DEPARTMENT OF HEALTH & HUMAN SERVICES

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National Cancer Institute
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Memorandum

Date: April 15, 1998

From: **Dr. Ihor J. Masnyk**
Project Officer

Subject: Technical Report

To: **Mr. Richard Hartmann**
Contracting Officer

Contractor: **Columbia University**

Contract number: **N02-CB-77032**

Reporting Period Covered: 01/01/98-03/31/98

Type of report: **Quarterly Progress Report**

I have reviewed the above mentioned technical progress report

[redacted] The report is satisfactory

[redacted] The report is unsatisfactory, see comments below

COMMENTS:

Signature of Project Officer

SUPPORT AND MANAGEMENT FOR THE PROJECT:
"EFFECTS OF THE CHERNOBYL ACCIDENT ON THYROID CANCER AND LEUKEMIA/LYMPHOMA"
CONTRACT BETWEEN NATIONAL CANCER INSTITUTE AND THE TRUSTEES OF
COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK
QUARTERLY PROGRESS REPORTS, JANUARY 1, 1998 - MARCH 31, 1998

1. INTRODUCTION

The second three months of the contract focused on preparation for and execution of the first Columbia team on-site visit to Belarus and Ukraine. In summary, eight members of the Columbia team attended an orientation meeting at NCI headquarters on January 9, 1998, focusing on progress to date in the two thyroid studies.

On January 23, 1998, a training workshop was held at Columbia to sensitize members of the Columbia team to Belarus/Ukraine cultural and economic circumstances. Emphasis was placed on insights into ongoing political realities in the two countries as well as diplomatic responses to changing situations.

As scheduled by NCI, the first trip to Belarus and Ukraine began on February 2, 1998. Although all members of the team were unable to participate in the first trip, those that were a part of this visit returned with a greater understanding of the scope and the difficulties of this project. Upon return, the leukemia study questionnaire was given to Dr. Svetlana Kokoreva, a member of the core Columbia administrative team, for translation along with other pertinent documents. The core administrative team proceeded to systematize the information flow within the Columbia component of the studies and finalize the Utah subcontract. Each of these items is now presented in more detail.

2. JANUARY 9, 1998 THYROID ORIENTATION AT NCI

The following members of the Columbia team giving technical support to the thyroid projects in Belarus and Ukraine attended an orientation meeting at NCI: Professor David Burch, Drs. Judith

Fayter, Daniel Fink, Ellen Greenebaum, Edward Haskell, Daniel Heitjan, Geoffrey Howe and Robert McConnell. NCI provided the Columbia thyroid team with an overview of progress to date. The presentation began with Dr. Ihor Masnyk's description of the cultural differences between Belarus/Ukraine and the United States, as they impact the studies. Dr. Gil Beebe, of the NCI, then gave an overview of progress to date, and other members of NCI and their consultants discussed issues related to their specialties, Drs. Randy Brill (ultrasonography); Andre Bouville (dosimetry); Herman Mitchell (establishment of data coordinating centers in both projects); Jack Robbins (endocrinology and pathology issues); and Everett Mincey (clinical laboratory management and quality control issues).

Dr. Bruce Wacholz of NCI gave an overview of his perspective of the importance of the studies between the United States and Belarus/Ukraine.

3. JANUARY 23, 1998 WORKSHOP ON SENSITIVITY TO CULTURAL AND ECONOMIC CONDITIONS IN THE FORMER SOVIET UNION

In order to prepare the Columbia team for their upcoming trip to Belarus/Ukraine, this meeting began with other Columbia faculty members' experiences in conducting studies in Eastern Europe. One of our advisors, Dr. Joseph Graziano, Professor of Public Health and Pharmacology, spoke about his work on the 20-year Yugoslavian lead study; and Dr.Basil Worgul, one of our co-investigators and Professor of Ophthalmology, discussed his research on the occurrence of cataracts occurring in liquidators as a result of the Chernobyl accident. Both stressed the need for personal contacts and respect for the traditions of the host nations.

Dr. Mark von Hagen, another of our advisors, and Professor of History and Director of the Harriman Institute, added the perspective of the interactions within the Former Soviet Union as they relate to increased contact with western science and culture.

Drs. Svetlana Kokoreva, Frank Miller, another advisor and Associate Professor and Chairman, Department of Slavic Languages, and Lydia Zablotska, Staff Associate and a member of our administrative staff, concentrated on the protocols of social and professional interactions in Belarus and Ukraine. Each of these subjects is presented in greater detail in Appendix I.

4. JANUARY 31, 1998 TO FEBRUARY 13, 1998 TRIP TO BELARUS AND UKRAINE

Members of the Columbia team (Professor David Burch, Drs. Daniel Fink, Charles Geard, Edward Haskell, Daniel Heitjan, Robert McConnell and Robert Reiss) together with NCI scientific personnel and consultants (Drs. Gil Beebe, Andre Bouville, Randy Brill, Ihor Masnyk, Everett Mincey, Herman Mitchell and Jack Robbins) traveled to Belarus and Ukraine for an on-site visit. This trip provided the NCI the opportunity to introduce the new members of the team to their scientific counterparts in the thyroid studies in Belarus and Ukraine and the leukemia study in Ukraine. The focus of the trip was to update the American scientific personnel with progress to date in the three studies and allow the new members of the team the opportunity to interact with their scientific counterparts in order to enable them to recognize, analyze and respond to the ongoing needs of the studies. In particular, scientific personnel were thus able to offer practical suggestions to expedite the execution of the studies. Upon their return to the United States, members of the Columbia team prepared individual trip reports (see Appendix 2) outlining their respective experiences. Each trip report reflects the expertise of the individual scientist and includes his recommendations as they relate to his specialty. A brief summary of the observations and recommendations made by the relevant participants follows.

5. STUDY OF THYROID CANCER AND OTHER THYROID DISEASES IN BELARUS FOLLOWING THE CHERNOBYL ACCIDENT: SUMMARY OF INDIVIDUAL TRIP REPORTS

5.1 Professor J. David Burch, Epidemiology and Fieldwork

In meetings with Dr. Elena Buglova, Head of the Epidemiology Group at the Clinical Institute of Radiation Medicine and Endocrinology, Professor Burch identified a number of problem areas and offered alternative strategies to improve the identification and follow-up of the cohort:

i. ***Obtaining current addresses for non-respondents and those with current addresses not known***

- suggestions include: utilization of passport and school records and felchers (public health nurses) at the local level.

ii. ***Change orientation of approach to cohort members:***

- simplification of correspondence with cohort members; informing cohort members of mobile team schedules; concentration of mobile teams' efforts in local areas with high density of identified cohort members; utilization of answering machine to allow cohort members easier participation.

iii. ***Implementation of incentives for study participation:***

- thank you letters; token gifts for children; study logo with which cohort members can identify.

iv. ***Training and quality control:***

- interviewer training; standardized approach; monitoring of interviews.

v. ***In utero study:***

- develop database and questionnaire

vi. ***Establish coordinating committee with one representative from each subgroup in the study.***

More detailed recomendations are found in David Burch's complete trip report (see Appendix 2, Part A).

5.2 Dr. Robert McConnell - Endocrinology

In meetings with Dr. V. Khlyavich, who does the fine needle aspiration biopsies (FNAB), Dr. McConnell noted procedural and quality control problems which need to be addressed.

i. ***Quality control:***

- Procedures to ensure adequate sampling of thyroid nodules

ii. ***Equipment:***

- Staining and slide examination time would be much reduced by providing needed equipment outlined in Dr. McConnell's trip report.
- Investigate service contracts for equipment.

iii. ***Laboratory reports and procedures:***

- Revision of laboratory report summary to provide anatomic location of aspirated nodules and indicate if FNAB was done.
- Obtain calcium levels before ultrasonogram.

iv. ***Solidify working relationships:***

- Participate in collaborative study of the utility of color Doppler in selecting patients for surgery.
- Forms finalization and procedures for change need to be established.

v. ***Lack of reagents for the Abbott IMR is a major problem. (Dr. Fink worked with local Abbott "rep.")***

More detailed recommendations are found in Dr. McConnell's complete trip report (see Appendix 2, Part A).

5.3 Dr. Daniel Heitjan, Data Management and Biostatistics

In meetings with Artur Kuvshinnikow, Head of the Data Control Center (DCC), Dr. Heitjan observed that data entry and management systems were presently functioning well. Quality control and biostatistics, however, were areas that he identified as having potential problems.

i. ***Biostatistics support:***

- Identify scientists with aptitude for biostatistics for subsequent biostatistical training.
- Evaluate SAS geographic information system (GIS) component
- Acquire S-Plus statistical software package.

ii. ***Data and quality control:***

- Establish forms committee.
- Document procedures for changing forms in the data management operations manual.

More detailed recommendations are found in Dr. Heitjan's complete trip report (see Appendix 2, Part A).

5.4 Dr. Daniel Fink - Clinical Laboratory Management/Quality Control

In meetings with Dr. Petrenko, Dr. Fink identified a number of problem areas and proposed appropriate solutions.

i. ***Initiation of hormonal studies:***
   - T4, TSH testing, TPO and Thyroglobulin (TG).
   - Get testing underway on arrival of Abbott reagents, evaluate TPO and TG assays.

ii. ***Quality control:***
   - The Abbott reagent order should include quality control material.
   - Compare results of specimen analysis between Ukraine and Minsk, Columbia and Minsk.
   - Evaluate specimen storage procedures.
   - Establish a quality control council with representatives from all study groups to monitor completeness of data forms.

More detailed recommendations are found in Dr. Fink's complete trip report (see Appendix 2, Part A).

6. STUDY OF THYROID CANCER AND OTHER THYROID DISEASES IN UKRAINE FOLLOWING THE CHERNOBYL ACCIDENT; SUMMARY OF INDIVIDUAL TRIP REPORTS

6.1 Professor J. David Burch, Epidemiology and Fieldwork Procedures

In meetings with Dr. Anna Derevyenko, Head of the Epidemiology Group at the Institute of Endocrinology and Metabolism, Professor Burch identified a number of problem areas and offered alternative strategies to improve the identification and follow-up of the cohort in the "pilot" raion of Ivankiv:

i. ***Obtaining current addresses for non-respondents and other cohort members not presently located:***

   - Utilization of school records in addition to tracing through passport offices..

ii. ***Current study procedures in Ivankiv raion:***

- Need to continually monitor study procedures being followed by local area medical staff.

iii. ***Change orientation of approach to cohort members:***

- Simplification of correspondence with cohort members.
- Utilization of answering machine to allow cohort members easier participation; informing potential cohort members of availability of mobile examining teams in local areas; adding "postcard" to self-administered dosimetry form asking cohort members to aid in cohort member follow-up.

iv. ***Study questionnaire***

- ensure that Ukranian dosimetry questionnaire is as identical as possible to that being administered in Belarus

v. ***Implementation of incentives for study participation:***

- Thank you letters.
- Token gifts for children.
- Study logo with which cohort members can identify.

vi. ***Training and quality control:***

- Interviewer training stressing standardized approach.
- Monitoring of interviews.

vii. ***In utero study:***

- Develop database and questionnaire

viii. ***Coordinating committee***

- Establish a coordinating committee with one representative from each subgroup in the study.

More detailed recommendations are found in David Burch's complete trip report (see Appendix 2, Part B).

6.2 Dr. Daniel Heitjan, Data Management and Biostatistics

Meetings were held with V. (Slava) Derzhovets, head of the DCC and members of his team. Dr. Heitjan's interactions with this team and his observations of the physical site resulted in several conclusions:

i. ***Equipment:***
   - Computing equipment had not yet arrived.

ii. ***Recruitment of cohort:***
   - Redouble efforts to contact sampled cohort rather than expanding cohort by enrolling only subjects who are easy to contact.

iii. ***Biostatistics:***
   - Identification of a potential on-site biostatistician for intensive training

iv. ***Data and forms quality control:***
   - Utilize scanning for diagrams indicating site of lesions in palpation and ultrasound exam forms.
   - Additional training for interviewers.
   - Establishment of central data and forms quality control function.
   - Establish and document procedures for changing forms; this will include documentation of all changes and reasons for changes.

More detailed recommendations are found in Dr. Heitjan's complete trip report (see Appendix 2, Part B).

6.3 Dr. Robert McConnell - Endocrinology

After meeting with Dr. N. Tronko, the Director of Endocrinology and Metabolism and his Deputy, Dr. V.P. Tereshchenko, Dr. McConnell observed that the Ukraine study was still in the organizational phase and hampered by lack of equipment. The "pilot" study being carried out in the Ivankiv raion of the Kyiv Oblast has a 67% retrieval rate. The numbers from Narodichy and Ovruch

Oblasts are not as good. Dr. V.A. Oliynyk, Deputy Director of Clinical Work, confirmed that three mobile teams would be ready in 2-3 weeks.

Dr. O.V. Epshtein, Director of the Central Laboratory, described equipment still under customs seal and his need for vacutainers. Dr. T.I. Bogdanova, Head of the Morphology (Pathology) group has 23 cases of thyroid cancer (21 from the cohort) and her laboratory is "up and running."

Dr. McConnell then observed problem areas and possible solutions.

i. ***Foster interaction between Ukraine and U.S. scientists:***
   - Collaborative study between Drs. Bogdonova and E. Greenebaum of Columbia University.
   - Visit of American surgeon (possibly Dr. Paul LoGerfo, chief thyroid surgeon at the Presbyterian Hospital) to Kiev.

ii. ***Forms:***
   - Need for English version of clinical screening form.

iii. ***Laboratory procedures:***
   - The procedures used are efficient.
   - There was no visible evidence of criteria definition, quality assurance or a cytology form.
   - Standardization of pathology form between Ukraine and Belarus.
   - Implementation of use of Pathology Form immediately.

More details of his recommendations are included in his trip report (Appendix 2, Part B).

6.4 Dr. Daniel Fink - Clinical Laboratory Management/Quality Control

The discussion between Drs. Epshtein and Fink focused on laboratory issues and quality control.

i. ***Initiation of hormonal studies: TSH, T4, TPO and TG:***
   - Because screening of patients in significant numbers has not started yet, the replacement of Amberlite by Brahms reagents will not pose a problem.
   - Bring in Brahms reagents as soon as possible for full evaluation.

ii. ***Quality control:***

- The Brahms reagent order should include quality control procedures
- Compare results of specimen analysis between Ukraine and Belarus and Columbia and Kiev.
- Data entry mechanisms for study data should be tested; and data forms finalized and tested.

More details of his recommendations are included in his trip report (Appendix 2, Part B).

7. STUDY OF LEUKEMIA AND OTHER HEMATOLOGICAL DISEASES AMONG CLEAN-UP WORKERS FOLLOWING THE CHERNOBYL ACCIDENT: SUMMARY OF INDIVIDUAL TRIP REPORTS

7.1 Professor J. David Burch, Epidemiology and Fieldwork

Professor Burch reviewed study design, fieldwork procedures and progress to date with Dr. Natalia Gudzenko, Head of the Epidemiology Group at the Research Centre for Radiation Medicine, especially pertaining to Dniproptivsk Oblast which has been chosen as a "pilot" oblast. Problem areas were identified, which will need attention.

i. ***Finalize criteria for inclusion of cohort:***

- Natalia expressed the need to determine if clean-up workers who move from catchment area, or who were in the army, fire brigade and those employed at Chernobyl at the time of the accident, are eligible.

  NB: The definition of the cohort has been covered in detail in Dr. Howe's memorandum to Dr. Beebe, dated October 9, 1997 (see First Quarterly Report, Appendix 3); we have not transmitted this memorandum to our Ukrainian colleagues since we thought this should come directly from NCI.

ii. ***Study procedures for "pilot" Dniproptivsk Oblast:***

- Change introductory letter to liquidators; use of answering machine to facilitate participation by cohort members

iii. ***Active follow-up:***

- Initiate aid of local health nurses, thank you letters, newsletters, etc; add "postcard" to self-administered dosimetry form seeking cohort members help in maintaining contact.

iv. ***Passive follow-up:***

- Involve Ministry of Internal Affairs (Passport office); social benefit and certification of victims offices.

v. ***Interviewing procedures:***

- Pilot test questionnaires in Dniproptivsk Oblast; administer questionnaires in liquidators' homes and at polyclinics; continual monitoring of interviews; change questionnaire based on pilot testing.

More details of his recommendations are included in his trip report (Appendix 2, Part C).

7.2 Dr. Robert Reiss, Hematology and Pathology

Dr. Reiss, in his meetings with Drs. Finch, Klimenko and Dyagil, pursued a number of issues. Dr. Reiss' primary concern was his impression that Drs. Klimenko and Dyagil wished to exclude participation of the pathologists from the Oncology Institute, the latter being trained pathologists.

i. ***Laboratory procedures and facilities - need to emphasize that interactions between the Oncology Institute and the study are vital:***

- Laboratory facilities are marginal and there are currently no pathology facilities on site
- Need to rediscuss whether the working formulation classification for lymphomas is optimal for this study
- Full utilization of FAB classification of leukemia is dependent on a flow cytometer which Dr. Reiss was not able to evaluate
- There is currently an inadequate inventory system for sample storage.

More details of his recommendations are included in his trip report (Appendix 2, Part C).

7.3 Dr. Edward Haskell, EPR of Tooth Enamel

After meeting with Dr. Romanyenko, Dr. Haskell identified several problematic areas.

i. ***Customs:***

- Consider paying 100% duties for time-sensitive material that would have to be reordered and that would delay work.

ii. ***Dosimetry:***

- EPR measurement would be better evaluated if a photograph was taken of each tooth to show caries.
- Visit by Dr. Sergei Sholom to the University of Utah to verify the effects of caries and sample preparation procedures on accuracy of EPR dose measurements.

iii. ***Pilot questionnaire:***

- Establish affiliation of liquidators to enable assignment of doses to groups of individuals based on their units location and activities.
- Postcard questionnaire mailing successful.
- Utilize polyclinic cards to identify individuals with "liquidator" classification, but no registry number.
- Cross-check local authority records that assign "liquidator" status against names in the state registry.

iv. ***Description of EPR databases:***

- "Liquidator" tooth specimen availability is the first criteria of these studies and at present the availability level is low.
- Dr. Chumak described the database associated with the liquidators in relation to sample preparation, treatment methods, quantity and quality measured and amount remaining for future measurement.
- Another database demonstrated access to individual spectra, processed spectra, doses applied to samples and plots of the dose response curves for each sample.

A more detailed description of Dr. Haskell's observations is found in his trip report (see Appendix 2, Part C) and in the section of this progress report prepared by the University of Utah.

7.4 Dr. Charles Geard, Biological Dosimetry

As a result of his meetings with Drs. Chumak and Pilinskaya together with Drs. Finch and Reiss, Dr. Geard evaluated the biological dosimetry aspects of the study with particular attention to fluorescent *in situ* hybridization (FISH) technology, electron spin resonance (ESR) and laboratories and equipment.

i. ***FISH:***
   - Lack of supplies and equipment; poor refrigeration space.
   - Chromosomal studies possibly could be aligned with initial studies which use chromosomal biodosimetry to indicate high doses.
   - Could not evaluate laboratory due to lack of equipment.

ii. ***ESR:***
   - Laboratory is well organized with an established system for identifying and collecting teeth.

iii. ***FISH/ESR:***
   - Important to coordinate the two dosimetry programs so that optimal information can be achieved.
   - Biological dosimetry at the present time lags behind other dosimetry components.

A more detailed description of his report is included in Appendix 2, Part C.

8. MISCELLANEOUS ACTIVITIES AT COLUMBIA UNIVERSITY INCLUDE:

8.1 Dr. Kokoreva completed translation of the leukemia questionnaire (see Appendix 3) and business cards for the Columbia team in Russian/English and Ukranian/English were prepared. Additional software relating to the production of Cyrillic fonts and keyboards. were identified and purchased.

8.2 Dr. Lydia Zablotska and Ms. Sally Hodgson, Program Coordinator, collaborated on the beginning of a literature search and establishment of a basic library for the use of the Columbia team. Articles received from Drs. Masnyk and Beebe for distribution to the team become a part of this library.

8.3 Dr. Zablotska conducted a preliminary review of web sites related to Chernobyl, with the intention of linking to the upcoming NCP-Columbia Chernobyl site.

8.4 Ms. Hodgson worked with Todd Cole and Jose Diaz (Columbia University) to complete the Utah subcontract which is now in place.

9. PROPOSED WORK PLAN: April - June 1998

9.1 A meeting to review the February trip was delayed until Dr. Howe was able to attend. This meeting will be held prior to the upcoming May visit. This will provide investigators with an opportunity to confer about their impressions and recommendations from the first trip as well as formulate their goals for the upcoming visits.

9.2 There will be a trip to Ukraine from May 15-21, 1998, split between Dnipropetrovsk and Kiev. Professor Burch, from the Columbia team, will accompany Drs. Beebe, Finch, Masnyk, and Tirmarche of IPSN to Dnipropetrovsk to evaluate fieldwork procedures in the leukemia study of clean-up workers in this pilot area. At the same time, the dosimetry group will be in Kiev meeting with their counterparts to evaluate progress in this area. There will also be a trip to Kiev and Minsk during the period May 31, 1998 to June 11, 1998 to introduce additional members of the Columbia team to the study of thyroid cancer in Belarus and Ukraine (Drs. Fayter and Greenebaum) who will be accompanied by Professor Burch and/or Dr. Howe and Dr. McConnell. The trip to Kiev and Minsk will focus on progress in the studies to date and the planning of new activities in the immediate future.

9.3 Sally Hodgson plans further work with the web site. A professional was located to potentially assist in the development of the web site who is familiar with security needs, document linkages and site linkages. Our goal is to establish a web site with a dedicated computer, already in place, that will be password secure. This will allow scanning of documents for downloading at NCI, Belarus, Ukraine or Utah and provide a convenient communications channel. This site will also have links for electronic transfer to additional sites which can be used for more detailed information or discussions. This would simplify communications between the multiple centers.

9.4 With the Utah subcontract now in place, Ms. Hodgson will make preliminary projections for fiscal close of Year 1.

9.5 As suggested by Daniel Heitjan a project staff directory is underway and there are plans to include brief descriptions of areas of expertise where possible. The possibility of working with a consultant to make this available at the web site and updatable by designated personnel at each location will be examined. Standardized spelling of the English transliteration of Russian names would be especially helpful in this endeavor.

9.6. Drs. Svetlana Kokoreva and Lydia Zablotska will continue translating scientific documents and questionnaires/forms for the team.

9.7 Dr. Lydia Zablotska will continue her work on the literature search with recommendations for books and articles to add to the library.

9.8 As suggested by NCI, preliminary preparations for a joint meeting of investigators from NCI and Columbia will be made.

9.9 Professor Burch will continue his work on existing questionnaires/forms and make suggestions for changes, where appropriate and feasible.

9.10 We anticipate that one or more individuals from Belarus and/or Ukraine will be identified by NCI for training during this period. We would plan to develop appropriate training schedules for these individuals in consultation with NCI and would have them make the necessary logistical arrangements for the trainees.

9.11 We plan to develop a more systematic approach to the preparation of trip reports so that in the future, such reports follow a more systematic and uniform format.

10. SUBCONTRACT: SCIENTIFIC EFFORT BY THE UNIVERSITY OF UTAH

10.1 Dr. E. Haskell

This progress report covers the work of Dr. Haskell concerning EPR dosimetry in support of leukemia studies.

On a trip to Ukraine in February 1998, Dr. Haskell met with Drs. Chumak and Sholom to discuss recent findings from the Utah EPR laboratory concerning alterations in EPR dosimetric properties of carious teeth. Since many of the teeth analyzed in Dr. Chumak's laboratory are extracted because of the presence of large caries, this issue is of direct relevance to past and future EPR measurements. Dr. Chumak indicated that several of the issues had been directly addressed by experiments in his laboratory, however, re-examination of his data, in fact, confirmed several of the anomalies. All agreed that the issue requires more detailed investigation, and that a visit by Dr. Sholom to the Utah laboratory to confirm the recent Utah findings should be undertaken as soon as possible. It is possible that a two-month visit by Dr. Sholom will not fully dispel the concerns raised and that the issues will best be addressed through future contractual research. A decision to pursue this course of action will await the results of Dr. Sholom's visit. Details of the EPR effects requiring investigation are given in Dr. Haskell's trip report in the appendix.

As an interim precaution, it was recommended that photographic documentation be collected for all teeth examined, particularly those displaying visible caries.

Other matters discussed during the visit included the following. Details of these items are given in the attached trip report.

- Examination of the databases used for the EPR effort. The databases were well developed and up to date and provided immediate information on sample origin, status of EPR measurements, preparation procedures and quantity of sample remaining.

- Review of the pilot questionnaire mailed to liquidators. The purpose of the pilot project was to assess the ability of locating registry entrants on the basis of their addresses in the state registry and to assign affiliation of the time of cleanup. The results of the mailing were successful in terms of participant response; and modifications to the questionnaire were being formulated based on apparent confusion with some of the questions. Several additional means of identifying liquidators include the use of polyclinic cards to identify individuals with "liquidator" classification, but with no registry number, and a cross-check of local authority records that assign "liquidator" status against names in the state registry.

10.2 Dr. T. Straume

a) Dosimetry

As the subcontract between Columbia University and the University of Utah was finalized only a few days ago, our efforts in support of the subcontract will necessarily be greater during the second half of FT98 than during the first half.

At present, my principal roles in support of the subcontract appears to be three fold: provide iodine (esp. I-129) expertise in support of the thyroid studies, provide QA/oversight for the FISH

biodosimetry, and provide general expertise in retrospective dosimetry as needed for both the leukemia and thyroid studies.

Although I am only this month beginning to charge some of my time to this subcontract, I have begun efforts in two areas that support the Columbia/NCI Program.

I-129 Efforts

As you know, I direct the DOE project with the aim to reconstruct radioiodine deposition from the Chernobyl accident in Belarus. The DOE project is scheduled to be completed on June 30, 1998. The reconstruction of iodine deposition is required to provide accurate thyroid doses and will improve the thyroid cancer risk estimates to be obtained from the epidemiology studies. The DOE study will provide a deposition map for iodine for the entire country of Belarus. However, it will not provide sufficient detail in all regions thus additional measurements will have to be made in support of the Columbia/NCI thyroid cancer studies.

Importantly, as a part of the DOE project, I am now setting up an iodine laboratory in Minsk in the Institute of Radiation Medicine and Endocrinology. I have already trained a Minsk chemist and have purchased and shipped all of the required lab equipment to Mink. This lab should soon be ready to extract iodine from environmental samples (e.g., soil). We have also developed soil sampling and processing protocols. This means that the additional soil samples required for the thyroid studies in regions such as Brest (and other regions of interest) can be collected and processed at relatively low cost by Minsk scientists with only QA, oversight, and AMS measurement by Utah. That is, the high-cost investments of training and equipment have already been completed under the DOE project.

During the remainder of this year, I would like to work with you to define the regions where additional iodine measurements are required in support of the thyroid cancer studies, and develop a plan for obtaining, processing, and measuring the samples. Such a plan should be coordinated with the DOE effort.

b) QA for Biodosimetry

During the past couple of months, I have performed QA on FISH biodosimetry data from Chumak's lab. These are data obtained by Kiev cytogeneticist, Dr. Maria Pilinskya, for Chernobyl workers exposed to various levels of radiation. There were three highly exposed groups with acute radiation syndromes (ARS I, ARS II, and ARS III), one group of liquidators, one group of Sarcophagus workers, and an unexposed control. Importantly, the ARS groups had independent dosimetry estimates that could be compared with the FISH biodosimetry estimates. Biodosimetry studies such as those on whole-body exposed Chernobyl workers are important in helping to define the doses for the leukemia studies. These results will soon be prepared for publication. (I will provide a preprint when available.)

Also, I am working with Chumak and others to compare FISH and EPR results from selected Chernobyl workers to gain a better understanding of how the two methods compare in the same individual and thus provide a basis for measurement validation of the dose reconstruction models. We will prepare a paper on this work as well, which I will provide when available.

During the remainder of this year, I recommended that we develop a plan for using the available retrospective dosimeters to validate and improve dose reconstruction models. It is important now, at the beginning of this program, to carefully define the dosimetry validation and uncertainty analysis needs. FISH, EPR, and other retrospective dosimetry methods can be used to accomplish this but must be carefully focused on the critical issues. In part, this is because of the limited number of individuals that can be evaluated using biodosimetry, hence, those individuals that are evaluated must be selected very carefully to maximize the information gained.

APPENDIX 1

January 23, 1998

Sensitivity Training Meeting for Chernobyl Technical Support Contract

January 23, 1998

Sensitivity Training Meeting for Chernobyl Technical Support Contract

Those in attendance:

Charles	Geard	Biological Dosimetry
Joseph	Graziano	Consultant
Ellen	Greenebaum	Cytology, Pathology
Daniel	Heitjan	Statistics, Data Management
Sally	Hodgson	Program Coordinator
Daniel	Illian	Meeting Support
Svetlana	Kokoreva	Administrative Assistant
Anne	Matsushima	Pathology, Clinical Lab Management
Robert	McConnell	Endocrinolgy
Frank	Miller	Chair, Dept. of Slavic Languages
Robert	Reiss	Hematology, Pathology
Anne	Schein	Administrative Asst. to Dr. Howe
Mark	VonHagen	Director, Harriman Institute
Basil	Worgul	Radiation Biology
Lydia	Zablotska	Staff Associate

The meeting was called to order by J. David Burch with some short welcoming remarks and introduction of Dr. Joseph Graziano, the first scheduled presenter.

10:15 AM "The Yugoslavia Prospective Pb Study: the Agony and the Ecstasy of International Collaborative Research"

Dr. Joseph Graziano, Professor and Head
Division of Environmental Health Sciences
Columbia School of Public Health.

Dr. Graziano highlighted the similarities of his work over the last 20 years in Yugoslavia with the planned work in Belarus and Ukraine. He noted problems of interfacing with changing governmental entities, difficulty in establishing credibility for United States long term interest, sensitivity of the Yugoslavian scientists to U.S. team's perceived expertise in problem assessment or solving and the frustrations of bureaucratic delays, currency devaluation, transportation problems, and other intrinsic Third World conditions.

In describing his long association with Yugoslavia Dr. Graziano stressed the importance of personal relationships with the scientists. It is through establishing personal credibility and then personal friendships with Yugoslavian colleagues that Dr. Graziano and other members of his team were able to maintain the momentum needed to complete twenty years of research. Additionally, Dr. Graziano found that, without direct personal communication on at least a weekly basis, scientific work in Yugoslavia unraveled. On every Tuesday afternoon over the past twenty years Dr. Graziano scheduled a telephone conference with colleagues in Yugoslavia. He has found this scheduled time immensely valuable in coordinating activities and in illustrating the importance of the Yugoslavian study to the U.S. team which helps to ensure that work continues between visits.

This cohort study monitored children over many years. In order to ensure high rates of continued response each child was given an age appropriate gift at each visit and

their parents were given the equivalent of approximately US $5.00. It was suggested that we look into the possibilities of also providing incentives for follow-up visits. Additionally, some Yugoslavian doctors were selected to be a part of the 'core team'. These doctors were placed on an annual salary and paid approximate US$1,200 - 4,300. Without this 'core team' Dr. Graziano felt it would be extremely difficult to maintain a study. Selecting some scientists for pay and others for no pay creates hard feelings and requires careful study before making a decision, however, the long term benefits outweigh the difficulties.

10:45 AM "Experiences and Lessons to Be Learned from the Ukrainian Ocular Study (UACOS) and How They Relate to a Large Joint Study"

Dr. Basil Worgul, Professor and Director of the
Eye Radiation and Environmental Research Laboratory
Department of Ophtalmology, Columbia University

Following Dr. Graziano, Dr. Basil Worgul reported on his current Ukrainian study on the effects of Chernobyl as evidenced by the development of cataracts in the 'Liquidators'. He began by describing the Chernobyl accident, areas of various contamination, and his current NCI study.

This year Dr. Worgul's study is evaluating 6,000 Liquidators for cataracts. About 1,000 cataracts were removed in Liquidators this year and ten years from now they expect 10,000 cataracts to require surgery. He described his research team and their goals which include helping to anticipate future medical facility requirements.

Dr. Worgul showed a diagram of the organizational structure of his study. In each section there are Americans and Ukrainians identified as responsible for the work scheduled by the team. Dr. Worgul reiterated Dr. Graziano's statements outlining the importance of maintaining constant contact and feedback as well as forming a "core team".

Dr. Worgul also stressed the importance of personal connections and personal relationships in accomplishing the research goals of a study. As his study developed he found it extremely beneficial to pay the scientists involved in the study and also to arrange for visits to Columbia University, or other relevant sites, for training and special instruction. The foreign scientists wanted very much to visit the United States and during their visits they were able to work with other scientists on the same equipment provided to the study in their countries.

As Basil Worgul finished speaking about paying salaries and travel to the United States, Joe Graziano seconded his recommendations; stating that it mirrored his experiences in Yugoslavia and that the scientists there viewed the U.S. team as a lifeline to help them through an extremely difficult period in their history. Dr. Worgul agreed that Ukrainians and Belarusians did view his U.S. team as a lifeline during their difficult times. While it is difficult to select the 'core team', both Drs. Graziano and Worgul found it necessary to select a team and find a mechanism to pay the team in order to complete the research goals of their projects. It is not unusual for workers to go 6 or 8 months without paychecks and, without financial incentives, it is unrealistic to expect them to concentrate on your work at the expense of finding a way to feed their families.

Basil Worgul also described the difficulties associated with obtaining Chernobyl Registries. He stated that the Registries were taken back to the provinces with the liquidators as they returned home which scattered the registries across the Former Soviet Union (FSU) making them very difficult to obtain.

Dr. Worgul then spoke about formal entry and exit procedures for both countries. He explained that 2-3 years ago customs was unorganized and it was possible to bring in and take out pretty much whatever was needed. However, today he would find it dangerous to attempt to exit either country with any item not declared at the border. Upon entry each visitor will be asked to complete a sheet listing any gold, electronic or other valuable items they are bringing into the country and it is necessary to make a

complete list. Upon exit each visitor will be forced to pay duty on items acquired while a visitor, which includes any valuable items not declared at entry. Also, he recommended making no attempt to take any art work out of the country (with the exception of items made to sell to tourists) as it would be confiscated at the border.

11:30 AM "Doing Business after the Soviet Union"

Dr. Mark Von Hagen, Professor and Director
The Harriman Institute, Columbia University

Dr. Von Hagen's experiences were similar to Drs. Worgul and Graziano. The breakup of the Soviet Union created many opportunities but also caused many problems. He expressed his opinion that a successful program would depend on integrating key Ukrainian and Belarusian scientists into the National Cancer Institute research team. He felt that training visits to Western research sites would provide incentives for a long term program as well as providing an opportunity to teach uniform procedures.

12:15 "Basics of Social Conventions and Business Protocol in Ukraine and Belarus"

Dr. Svetlana Kokoreva
Administrative Assistant
Chernobyl Technical Support Team
Columbia School of Public Health

Dr. Kokoreva first focused on the changes since independence and emphasized that Ukrainians/Belarussians are not Russians. Both Ukrainians and Belarusians take great pride in their independence and do not want to be referred to as Russians. Ukrainian and Belarusian are the formal languages and while Russian is spoken in both countries formal communications should be in the language of the country. As a visitor attempts to speak in Russian/Ukrainian/Belarusian will all be appreciated, but the native

Ukrainian/Belarusian will respect your acknowledgment that their country is separate and apart from Russia. Russia is viewed as the Province that demanded the resources of all other parts of the Former Soviet Union by many of the FSU countries and Moscow as the City that drained the provinces dry.

Next Dr. Kokoreva reviewed some basic business protocols which include the need to honor the hierarchy of the established institutions. Going to the "top boss" to achieve your goals will increase your chances for success appreciably. Also, realizing that "no" is the beginning of a negotiation rather than the end of business is extremely important. When faced with an apparent decision that there is "no possible way" that your recommendation can be implemented, it is necessary to ask "Why not ?" and present other possible solutions to keep the discussion open.

Personal contact in business and the advisability of personal introductions was stressed. The formal official level is never enough to get work done. It is imperative to establish good working relationships with the people conducting the work and to maintain very frequent contact. Without frequent personal contact work lapses between visits and even with extensive written protocols and agreements you "won't get much done".

Practical Tips: Meals are breakfast, dinner and supper with the major meal of the day dinner. Lunch/Dinner time is between 1:00-3:00 PM and it is considered rude to schedule meetings during that time. As even stores close for dinner it is unlikely that you would find your counterparts available for telephone conversations during those hours.

When traveling it is best to give yourself extra time to fill out forms and pass through customs as it is difficult to judge how much time you may need.

Bringing everyday supplies with you will help to avoid searching for an item in either Kiev or Minsk. While you may be able to obtain health and cosmetic aides you will waste time looking for them and they will be more expensive.

Some indigenous customs were described:

- Flowers - always bring an odd number (even numbers of flowers are only for funerals).
- Flowers and a bottle of wine or other small gift are expected when attending a dinner party at someone's house.
- Don't shake hands over the doorstep and always take off your gloves.
- If you smoke, don't get a light from a candle on the table.
- Men must remove hats or caps once they come into the office or home.
- Don't leave an empty bottle (doesn't matter what was in it) on the table.

12:30 PM "Social Conventions and More - Another Point of View"

Dr. Frank Miller, Professor and Chair of the
Department of Slavic Languages
Columbia University

Dr. Frank Miller described his own experiences and some other customs. Among those he discussed was the Russian/Ukrainian/Belarusian tradition of giving and receiving gifts. When meeting a colleague with whom you expect to establish a working relationship a gift such as a coffee cup or a T-Shirt may be appropriate. Certainly, when accepting the hospitality of a native it is customary to bring a small gift and most likely to also receive a small gift. Gifts can be coffee cups with Columbia logos, T-Shirts, key chains, professional books, books with pictures of the United States, small toys for children, a CD or other items from the US that you feel would interest someone in these countries.

12:45 PM "Basics of Professional Etiquette"

Dr. Lydia Zablotska
Staff Associate
Chernobyl Technical Support Team
Columbia University

Dr. Zablotska, who was a practicing physician in Ukraine prior to coming to the United States to continue her studies, discussed differences in professional behavior and business etiquette. The business environment in Belarus and Ukraine is more formal

and goes back to our own business environment of the 1950s. Dress codes advise skirts for women and expect corporate meeting business attire. Smoking is socially acceptable and is allowed in many situations.

Ukrainian etiquette at first introduction differs from the American form. Men should wait for women to extend their hands first and they may not choose to do so. It is not acceptable to use first names in a business setting until a Ukrainian partner does. Using first names is a sign of a true friendship and is considered very important.

The work schedule of physicians and health care administrators differs from ours. Usually, official business hours do not start until 9 a.m. However, at that time, it is customary for them to attend business meetings going on until 10 a.m. It is advisable not to schedule any meetings at that time as it may be uncomfortable for Ukrainian/Belorussian partners. Time from 2 to 3 p.m. is taken off for dinner/lunch.

Dr. Zablotska explained that health care in Ukraine and Belarus is still a government-run business with all of its shortcomings and drawbacks. Physicians and scientists are controlled by a very rigid hierarchical administrative structure. It is, therefore, preferable to talk to those who are in charge and are able to make decisions. Be patient and do not expect quick decisions. It may be necessary to negotiate arrangements for a long time.

Her presentation finished with final remarks about good topics for informal conversations and showing respect to Ukrainian and Belorussian professionals. Dr. Zablotska invited project investigators to come to the Division of Epidemiology at Columbia University to consult available books on cultural differences, rules of professional etiquette and traveling in Eastern European countries.

J. David Burch and Sally Hodgson then responded to questions about NCI travel policies for obtaining visas, travel advances, tickets and reimbursement and the meeting was adjourned at 2:00 PM by Professor J. David Burch.

APPENDIX 2

Individual Trip Reports for Columbia Scientific Personnel Traveling to Belarus and Ukraine

SUPPORT AND MANAGEMENT FOR THE PROJECT:
"EFFECTS OF THE CHERNOBYL ACCIDENT ON THYROID CANCER AND LEUKEMIA/LYMPHOMA"
CONTRACT BETWEEN NATIONAL CANCER INSTITUTE AND THE TRUSTEES OF
COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK

Individual Trip Reports for Columbia Scientific Personnel Traveling to:

(A) Minsk, Belarus, February 2-4, 1998
Study of Thyroid Cancer and Other Thyroid Diseases in Belarus Following the Chernobyl Accident (BelAm)

(B) Kiev, Ukraine, February 5-9, 1998
Study of Thyroid Cancer and Other Thyroid Diseases in Ukraine Following the Chernobyl Accident

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(C) Kiev, Ukraine, February 10-12, 1998
Study of Leukemia and Other Hematological Diseases Among Clean-Up Workers in Ukraine Following the Chernobyl Accident

PART A

Minsk, Belarus, February 2-4, 1998

Study of Thyroid Cancer and Other Thyroid Diseases in Belarus Following the Chernobyl Accident (BelAm)

Trip reports for:

- Professor J. David Burch, Epidemiology and Fieldwork
- Dr. Robert McConnell, Endocrinology
- Dr. Daniel Heitjan, Data Management and Biostatistics
- Dr. Daniel Fink, Clinical Laboratory Management/Quality Control

J. DAVID BURCH, EPIDEMIOLOGY AND FIELDWORK
TRIP SUMMARY

February 2-4, 1998, Minsk, Belarus
Study of Thyroid Cancer and Other Thyroid Diseases in Belarus Following the Chernobyl Accident (BelAm)

The visit to the Clinical Institute of Radiation Medicine and Endocrinology began with a plenary session on the morning of February 2, 1998. The session was chaired by Dr. V.A. Stezhko, Director of BelAm Thyroid Disease Project. Various heads of departments involved in the project outlined progress to date on the implementation of the study, with 1997 essentially being a "pilot" year. Details of progress to date are included in the report "Implementation of Joint BelAm Scientific Protocol for Studies of Thyroid Cancer and Other Thyroid Diseases in Belarus Following the Chernobly Accident" which was supplied to us during our visit.

Meetings with Dr. Elena Buglova, Head of Laboratory of Radiation Hygiene and Risk Analysis (Head of Epidemiology Group)

I reviewed with Dr. Buglova (Elena) progress to date in the determination and follow-up of the cohort. A cohort of approximately 15,000 children (≤ 18 years of age at the time of the Chernobyl accident) has been identified in eight oblasts of Belarus, including Minsk. Of these, 8500 had measurements taken indicating high doses, and 7500 with low or medium doses. Current addresses of approximately 60% of the cohort (8477 potential cohort members) were ascertained through the Chernobyl Registry and the Chiefs of Medical Structure at the raion level, medical record departments of dispensaries and outpatient clinics.

Letters introducing the study to potential cohort members have been sent to those with known current addresses, resulting in 2200 who have agreed to participate with approximately 6200 unknown status or refused. The great majority of the 6200 unknown status cohort members who did not refuse either did not respond to the letter or indicated that they would not participate for various reasons (lack of money, in the Army, in jail, etc.). According to Elena, the absolute refusal rate is approximately 10%.

Suggestion: For the approximate 8000 potential cohort members who have no current address, the epidemiology group will contact the Ministry of Internal Affairs (Passport Offices) to allocate current addresses. Evidently, all citizens of Belarus 16 years of age and older are required to have a passport and information tor passport holders is constantly updated. I suggested to Elena that for those potential cohort members who did not respond at all to the letter, that their identifying information be given to the passport offices to determine current addresses as well.

Suggested Further Follow-up Procedures for Non-Respondents

In our discussion of current cohort member tracing and follow-up, it was evident that, unlike the West, reliance on contacting cohort members through the postal system is very problematic, i.e., people do ***not*** read their mail. In light of this fact, Elena and I developed alternate strategies to improve tracing and follow-up of potential cohort members with an emphasis on a more "grass roots" approach.

① As it is compulsory in Belarus to attend school until the age of 16 years, project staff may approach the school system at the raion level to ascertain, at the very least, the location of children in the cohort who are presently attending school.

② Evidently, within the raions there are personnel very much akin to our public health nurses (felchers) who could be asked to canvas neighborhoods in order to trace cohort members. If this is done, however, it is imperative that the felchers be instructed to follow a standard approach when explaining the study to potential cohort members.

③ For those cohort members who responded to the introductory letters that they would not participate for a variety of reasons (lack of money for transportation to clinics, in the Army, in jail, etc.), those cohort members should be followed-up with letters and/or personal contact explaining to them that the BelAm project has instituted a mobile team that could come to the local areas in which the cohort members live to examine them. These letters would make it clear to potential

cohort members that there would be alternative dates for examinations offered to them to make it as convenient as possible for the cohort members to participate in the project.

④ A determination of the location at the raion level of the geographical areas with high numbers of current addresses should be undertaken, especially in conjunction with progress of ascertaining addresses through passport offices at the raion level.

⑤ Subsequent to the completion of this process (see 4 above), the mobile team would be able to concentrate their efforts in the areas with high concentrations of current addresses.

⑥ For cohort members who are found neither to be resident near centralized population centers in raions or who indicate that they do not have sufficient money to travel to these centers, the mobile team could, in fact, where efficient, travel to local villages and settlements to examine cohort members.

Letter of Introduction to Project for Entire Cohort

In keeping with the "grass roots" approach and after reviewing the current introduction letter to cohort members, a number of possible alternative strategies were discussed:

① The introductory letter could be changed to make it more "user friendly." Acknowledging the cultural differences between the West and Belarus, Elena and I agreed that the letter could be made more "user friendly" by simplifying medical terminology, emphasizing that only through the participation of cohort members will the project be successful, etc.

② The introductory letter should include a statement to the effect that if the cohort members have any questions about the study, they can telephone the study office, ***at their convenience***, to have their questions answered.

③ The inclusion of (2 above) will necessitate the acquisition of a telephone answering machine with a message asking what the best way would be for project staff to get in contact with cohort members.

④ In conjunction with the use of the mobile teams, the introductory letter (and any follow-up letters) should include information about when and where the mobile team will be located in local areas to enable possible potential cohort members to choose the most convenient locale at which to be examined.

Self-Administered Dosimetry Form/Interview Form of Examination

Elena and I discussed the current version of the self-administered dosimetry form and agreed that the form could be simplified and that, for example, a question should be added asking who answered the questions and who, besides this person, helped in answering the questions and which questions that person helped answer. The dosimetric questionnaire administered to participating cohort members was also not available to me in English.

Suggestion: I informed Elena that I would look at it and suggest relevant changes where necessary.

Continued Follow-up of Established Cohort

Elena and I discussed ideas for the continued follow-up of the cohort. We came up with a number of suggestions. Our overall approach to follow-up is one of establishing a "living cohort."

① Send "thank you" letters to cohort members thanking them for their participation in the BelAm project.

② Send letters to participating cohort members informing them of progress in the study.

③ Give small token gifts to cohort members (especially children) when they attend clinics or the mobile team for examinations.

④ Develop a logo for the study with which cohort members could identify. This logo could be affixed to all correspondence sent to cohort members and could be put on coffee mugs, tee shirts, etc., which could be given as token gifts.

Training and Quality Control of Dosimetric Interviewing

Elena and I agreed that it is essential that all BelAm project staff who are responsible for interviewing cohort members (or their parents) be trained to do so using a standard interviewers' manual. Additionally, I suggested that interviewers should be regularly observed administering questionnaires to ensure, as far as possible, that interviewers are adhering to the standard interview approach. A sub-sample of interviewed cohort members should be re-interviewed in order to compare responses with the original interview.

In Utero Study

Very little time was spent discussing the planned in utero cohort study. However, I suggested that an initial database of exposed in utero children be established and that follow-up procedures for this cohort could include many elements of that used in the childhood cohort in order to determine current addresses and ensure continued follow-up.

Summary

Overall, I found Elena to be very enthusiastic about the project but hampered somewhat by the organizational structure of the BelAm project, i.e., the seemingly poor communication between the subdivisions of the project.

Suggestions: I would strongly recommend that a coordinating committee with one member from each subspecialty in the study be established and meet regularly so that all subspecialties can focus more clearly on the overall objectives of the study and are aware of on-going activities in each subdivision.

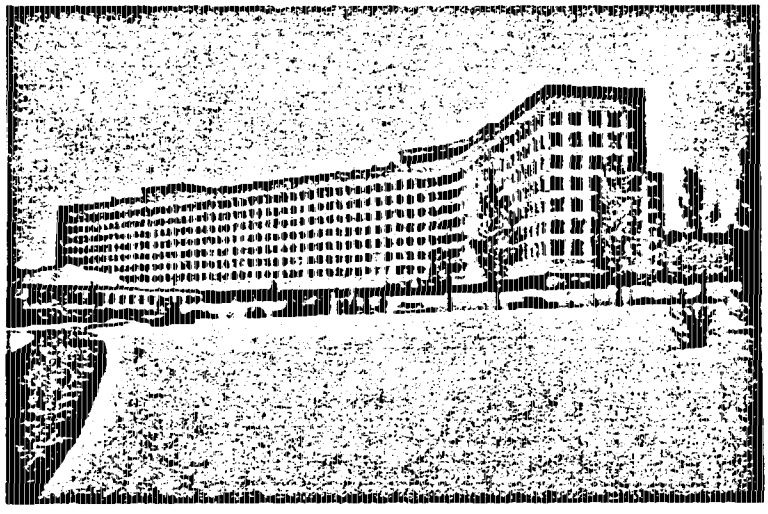
Dr. Robert J. McConnell
Endocrinology

Study of Thyroid Cancer and Other Thyroid Diseases in Belarus Following the Chernobyl Accident (BelAm)

February 2 - 4, 1998
Minsk, Belarus

1February1998: After a false start on Lufthansa, a restful flight on Singapore Air, and a long layover in Frankfurt, Belavia deposited us safely in snow-shrouded Minsk. The rooms at the Hotel Planeta are adequate and our safety is assured by the militia camped out in the lobby.

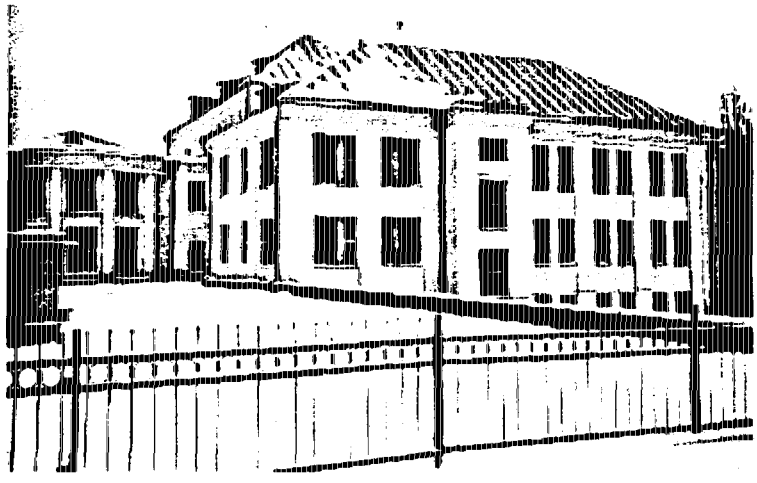
Memo: Lufthansa is not as organized as they would have one believe and Singapore Air flies empty, allowing you to lie down and sleep for a few hours.



Clinical Institute of Radiation Medicine and Endocrinology

2 February1998: The visit to the Clinical Institute of Radiation Medicine and Endocrinology began with a plenary session presided over by Dr. V. A. Stezhko, Director of the BelAm Thyroid Disease Project. Highlights of 1997 (a "pilot" year) were reviewed and it is clear that the Belarussians are still trying to find ways to implement the study. Although almost 60 % of the high dose group have been identified, they require a mobile screening team (which could double the number of subjects examined), more epidemiologists, and expansion of the operations in the Gomel oblast (where the largest

number of subjects reside). Ideally, screening would take place in the early spring, before the planting season and summer holidays. Tasks for 1998 include: (1). Identification and location of 8000 members of the cohort; (2). Implementation of the mobile screening team (they require a suitable "box " to transport the ultrasonogram and MOD drive); (3) Arrangement for screening to begin in Gomel; (4). Delivery of reagents (no thyroid function tests currently done due to lack of reagents from Abbott). A schedule for the visit was then set (but not in stone as it was quite fluid and changed several times each day, often for no apparent reason).



Minsk Dispensary

Gil Beebe, who had been feeling poorly since arrival, suddenly became too weak to stand and needed to be taken to the Minsk Dispensary, which is headed by Dr. V. A. Rzheutski (a very charming man). Although the whole of the afternoon was spent getting Dr. Beebe admitted to the Aksakovtchina Clinic, the process provided invaluable insight into the workings of the Belarussian medical system. Although their technology is about 25 years old, it can be used efficiently (if proper motivation is applied).

Memo: It would help to have uniform spellings of names (e.g., Stezko vs. Stezhko; Rzheutski vs. Rzeutsky). Form is more important than substance (this holds true for the Ukraine, too). Remember to "buckle up" in the front seat, since traffic police are everywhere and random checks are common (we were stopped and fined 50,000 rubles).

3 February 1998: Visited the Dispensary accompanied by Drs. Robbins and Brill, meeting Dr. V. Khlyavich who does the ultrasound-guided fine needle aspiration biopsy (FNAB), usually with a 25 gauge needle. Although they do up to 200/month, we did not observe their technique. Unlike in Kyiv (where a cytopathology technician screens all slides), the Belarussians do not check for an adequate sample and it takes a minimum of 30 minutes to stain and examine the slides. Dr. Khlyavich requires: (1). A linear transducer for performing the FNAB; (2). An extra transducer as a "backup" (they are fragile); (3) Water

bath kits; (4). Surge protectors x 3; (5). Tips on how to screen for adequate sampling quickly and efficiently (Dr. E. Greenebaum could help with this).

Dr. V. A. Rzheutski

Memo: Dr. Khlyavich is eager to learn about our procedures at CPMC (I hope that he is not too disappointed to learn that his techniques are superior to ours!). Servicing the equipment is a great challenge. Could a service contract be funded under the Columbia University grant?

4 February 1998: Back at the Dispensary today, meeting with Dr. Khlyavich and Dr. A. A. Romanovsky, who is based at the Aksakovtchina Clinic (where they have done over 700 FNABs in the last 3 years). Thyroid function tests are not done routinely on cohort members, except for those patients sent to Dr. Demidchik for surgery. Rather, the blood is collected and "banked" for future study. If there is a "suspicion" of thyroid cancer (palpation, FNAB, ultrasonogram) or if there is a "moderate" goiter, the patient is referred to Aksakovtchina for further evaluation. Criteria for FNAB are adult subjects with dominant nodules over 1 cm diameter and children with nodules greater than 3 mm diameter or any patient with a "suspicion" of thyroid cancer on ultrasonogram (inhomogeneity, calcification, increased vascularity, lymphadenopathy, etc.). It comes as a great surprise that color doppler flow studies (which are not part of the protocol) have been done at the Dispensary for over 12 months and are one of the major criteria used to increase suspicion of thyroid cancer. Dr. Rzheutski has been "borrowing" an Acuson unit from cardiology and requests that we purchase one for his personal use. We agree that small cysts (less than 3 mm in diameter) do not require referral to Aksakovtchina and that the Summary be changed to reflect the anatomic location of aspirated nodules (and if a FNAB was even done).

Drs. Romanovsky, Khlyavich, and McConnell

Memo: Parallel universes (like the color doppler) exist and unless one asks a direct question they will remain hidden. A good way to solidify a working relationship with Dr. Rzheutski would be to take up his offer of a collaborative study of the utility of color doppler in selecting patients for surgery. It is not clear that careful screening is done for parathyroid abnormalities. Having the calcium level available **before** the ultrasonogram might help, especially if it was abnormally elevated. I should meet Drs. Drozd (ultrasound), Demidchik (surgery), and Cherstvoy (pathology) next visit.

Back at the Institute of Radiation Medicine and Endocrinology for the final plenary session. The results of the working groups are discussed and the salient points concerning clinical screening are: (1). An additional workstation will be necessary for simultaneous viewing of prior and current images (Mitchell) ; (2). Establishing a "final" version of the various forms should be a milestone for 1 Quarter 1998 (Robbins); (3). Revision of forms falls under Quality Assurance (QA; Mincey); (4). There is a need to "stabilize" the forms to facilitate data entry (Mitchell); (5). There should be flexibility built into the forms to allow for technological advances over the life span of the project (McConnell); (6). A 3-D ultrasonogram will be available this year (Brill); (7). A major problem is the lack of reagents for the Abbott IMX (Dr. D. Fink made progress in solving this by meeting with the local Abbott "rep"); urine iodine (over 1200 have been done by Dr. S. V. Petrenko) and the ionized calcium are up and running; the mobile units should also perform ionized calcium (Mincey).

At the conclusion of the session, Dr. S. Yamashita of the Sasakawa Memorial Health Foundation (based in Gomel) marched in and took over. His group, which is examining about 40 patients each day, is planning to digitalize ultrasonogram images and transmit

them back to Nagasaki via satellite. The Sasakawa study will end its current phase in the year 2000 and their data could be made available to BelAm at that time. To facilitate this exchange, he proposes "coordinating" our parallel studies from the present time forward, including use of the same laboratory equipment.

Memo: There should routinely be a group visit prior to the final plenary session so that we coordinate our suggestions and present a united front (Dr. Mitchell's remarks about "stabilizing" forms was directed primarily towards dosimetry, but misinterpreted as applying to all working groups). Dr. Yamashita's offer to turn over his data sounds "too good to be true." We might get more done by having "working lunches" with our Belarussian colleagues.

Date sent: **Thu, 12 Mar 1998 16:27:24 -0500 (EST)**
From: **John David Burch <jdb32@columbia.edu>**
To: **sja1@columbia.edu**
Subject: **trip report, Minsk thyroid project, 98.02 (fwd)**

---------- Forwarded message ----------
Date: Mon, 9 Mar 1998 10:19:26 -0500
From: "Dr. Heitjan" <dheitjan@vanryzin.cpmc.columbia.edu>
To: jdb32@columbia.edu
Subject: trip report, Minsk thyroid project, 98.02

TRIP REPORT: BELARUS THYROID PROJECT
DATA MANAGEMENT AND ANALYSIS
MINSK, 98.02.01--98.02.04

Daniel F. Heitjan, PhD

Data Coordinating Center

Artur Kuvshinnikov, the head of the DCC, was present on Monday and Tuesday but was out sick on Wednesday, the final day of the visit. I earned a lot in the first two days but not so much on Wednesday.

The DCC appeared to be competently staffed and adequately equipped to handle the anticipated flow of data. Data entry and management systems were in place and functioning well. Mr. Kuvshinnikov demonstrated some quality control reporting programs that he had written. They represent a good start but more needs to be done.

Biostatistics Support

At the moment, the project is long on technology yet short on experience and quantitative research skills. A particular area of weakness is biostatistics; it appears that nobody in Minsk has much training in this area. Although the project does not at the moment require a full-time biostatistician, over time the need for someone with these skills will only increase. For example, we may soon wish to look for time trends in subject demographics or lab values, or do

preliminary analyses relating radiation dose to the presence of thyroid pathologies. Even if we are not yet ready to execute serious analyses of this kind, the preparation and execution of "dry-run" analyses can be an important quality-control device. The sooner we start, the better.

The existing computer hardware in Minsk is adequate for performing statistical analysis, although as the project grows we may need to acquire a dedicated computer. The DCC has SAS software, but the license expired without ever being used. Note that SAS has a geographic information system (GIS) component. I have not used it, but I suggest we evaluate its capabilities before purchasing some other GIS product. I suggest we also acquire S-Plus statistical software, a package that provides a more flexible programming environment and superior graphics capabilities.

Most importantly, we need to identify someone in the DCC who will serve as the on-site project biostatistician. This person should receive training, either by distance education or summer courses in the US, and be equipped with a core biostatistics library and adequate computer hardware and software. This project statistician will then be in a position to provide expert consultation on the spot with backup and guidance from the US.

Data and Forms Quality Control

Despite the generally sound accomplishments of the DCC, it seems that the various branches of the study are not always cooperating closely. A case in point is the dosimetry group. Mr. Kuvshinnikov indicated that after the data entry screens had all been programmed in what was intended to be their final form, the dosimetry group changed the forms, not once but several times, without informing the DCC. Moreover the dosimetry group is not yet connected to the network, despite the fact that at least some of their staff are sitting in the same room as the DCC.

A centralized quality control function for forms and data is essential. If the project leaders have not already done so, I suggest that they establish a forms committee to review and approve all changes before they can be implemented by the DCC. This group should be chaired by Kuvshinnikov and include representatives from all parts

of the study. Procedures for changing forms, which will include detailed documentation of all changes, must be spelled out in the Data Management Operations Manual.

To: David Burch, MS, MPH
From: D. Fink, MD
Date: 3/5/98
Re: Draft Trip Report for February 1 - 10, 1998

Minsk

We reviewed the results of the urinary iodine testing program. Over 1200 specimens were analyzed to date. In addition, the Minsk laboratory tested urine specimens from a European laboratory. There was good agreement between the results obtained in the two laboratories.

On the other hand, the hormonal studies in Minsk have not gotten underway. The planned tests are TSH, T4, TPO, and Thyroglobulin (TG). Specimens have been collected from approximately 1200 patients and have been stored frozen for up to a year. No testing has been performed on these specimens. Aside from the impact on the study, this may have delayed the diagnosis of sub-clinical hypothyroidism or hyperthyroidism.

The project purchased an Abbott IMX to perform T4 and TSH testing. However, a lack of reagents prevented the testing of patient specimens. Dr. Mincey, Dr. Petrenko, and I met with the Minsk Abbott representative and issues related to shipping and payment seem to be resolved. Also, since the reagents on hand are due to expire in March, the Abbott representative agreed to ship the missing calibrator prior to receiving payment so that the reagents can be used before they expire.

The laboratory has not finalized the methods for TPO and Thyroglobulin. A RIA method for TPO and TG will be performed using labeled antibody and the gamma counter available in the laboratory. Local reagents or reagents from a US manufacturer with a European distributor are being considered. These reagents have not been fully evaluated yet and testing can not begin until the evaluation is completed. There is not quality assurance program in place for the laboratory. The laboratory has no quality control materials, no proficiency samples, and no system to exchange samples with another laboratory. We discussed possible Quality Control options and obtaining QC material from Abbott for the IMX tests seemed to be the best option. We also discussed the possibility of comparing specimens between laboratories, including our laboratory in New York.

Recommendations:

1. Testing must begin as soon as possible.

2. The Abbott reagent order should include quality control material.

3. The assays for TPO and TG should be evaluated as soon as possible.

4. Samples for T4, TSH should be exchanged with the Clinical Laboratory to determine correlation between methods and to monitor values and quality of work.

5. If the shipping issues can be resolved, I have offered to send and/or receive specimens from the lab for comparison to results generated at Columbia. It may even be possible to enroll the lab in a US inter-laboratory comparison program.

6. I need to get an antibody catalog sent to Minsk for ?? company.

7. The effect of storage on the specimens should be evaluated by freezing several aliquots from new specimens for later analysis.

8. Urinary Iodine testing seems to be going forward well with a good comparison to results obtained in a European laboratory. Additional specimens should be exchanged on a periodic basis

Other observations

1. The study in Minsk seems to be generating data and screening patients.

2. Data collection forms need some minor improvements.

3. A review of a few cases revealed minor deficiencies in the accuracy and completeness of data. Each group in the study should establish an internal review of processes and data quality and then should report the findings to a quality assurance council consisting of representatives from all the groups.

4. If paper forms are to be preserved for 10-20 years, the low quality paper similar to newsprint now being used should be replaced with a higher quality paper that will not deteriorate over time.

5. Consideration should be given for using an optical disk based system for archiving and indexing bar coded data forms. Forms with bar-codes can be scanned and automatically indexed according to study number. Additional indexing could be performed manually. This would require much less space and effort in storing and retrieving data. Necessary forms can be reprinted when required.

PART B

Kiev, Ukraine, February 5-9, 1998

Study of Thyroid Cancer and Other Thyroid Diseases in Ukraine Following the Chernobyl Accident

Trip reports for:

- Professor J. David Burch, Epidemiology and Fieldwork
- Dr. Robert McConnell, Endocrinology
- Dr. Daniel Heitjan, Data Management and Biostatistics
- Dr. Daniel Fink, Clinical Laboratory Management/Quality Control

J. DAVID BURCH, EPIDEMIOLOGY AND FIELDWORK
February 5-9, 1998, Kiev, Ukraine

Study of Thyroid Cancer and Other Thyroid Diseases in Ukraine Following the Chernobyl Accident

Plenary Session, Thursday p.m., February 5, 1998 and Friday a.m., February 6, 1998
Institute of Endocrinology and Metabolism

The plenary session was chaired by Dr. N. Tronko, director, together with his deputy, Dr. V.P. Tereschenko. Various heads of departments in the study outlined progress to date on the implementation of milestones of the second quarter of the second year of work. The details of progress to date are included in the report "Implementation of Milestones of the 2nd Quarter of the Second Year of the Joint Ukrainian-American Scientific Project" which was supplied to us during our visit.

February 6-9, 1998, Meetings with Dr. Anna Derevyenko, Head of Epidemiology Group
I reviewed with Dr. Derevyenko in detail progress to date in the determination and follow-up of the cohort.

A 20,000 member cohort has been established, chosen by dose category with approximately 10,000 in the high dose group and 5,000 each in the lower dose groups. This cohort was resident in 1986 in eight raions of three oblasts: Kiev, Chernigon and Zhitomy. Of these, 7500-8000 were relocated and 14,200 still live in the eight raions.

Dr. Derevyenko outlined progress to date in determining current addresses for children living in the Ivankiv raion which has been chosen as a "pilot" raion to determine the feasibility of study procedures. She explained to me that current residence information has been established for approximately 70% (495) of the 737 potential cohort members who were ≤ 18 years old in 1986 in this raion through manual searching of records at the local hospitals and through the Chernobyl Registry; current addresses for 242 cohort members are as yet unknown.

Dr. Derevyenko informed me that the Ukrainian Ministry of Health requested from government officials via the passport office the current addresses of members of the cohort in Ivankiv raion (and all other raions) of children on the Institute of Radiation Medicine registry. This list contains identifying information such as surname, name, patronymic name, sex, date of birth, settlement and address. Anna informed me, however, that several of these identifiers are missing on many of the children's forms. At the time of the visit, Anna had not received any information back from the Ministry of Health as to the result of this request.

Suggestion: At this point in our discussion, Anna and I agreed that since a large percentage of the cohort will be, at present, below the age of 18 years, it would be a good idea to contact schools at all levels of administration to help in the identification of current addresses.

Fieldwork Procedures:

Following my orientation as to progress to date for the formation of the cohort and identification of current addresses, Anna and I discussed the fieldwork procedures presently being followed and those to be followed in the future.

① Ivankiv ("pilot") raion:

Letters of Introduction

Letters explaining and introducing the study have been sent to the 495 potential cohort members with known current addresses. Evidently, these letters are being sent to cohort members via public health nurses and physicians in local areas of the raion.

Suggestion: I am concerned that in the "pilot" work in Ivankiv raion, too much leeway is being given to the local area people who presumably are doing the project as a favor in sending the letters and talking to potential cohort members. Anna and I agreed that the local authorities should be provided with a standard introduction to the study.

Monitoring Visits

Furthermore, I suggested that Anna and/or Dr. Tereshchenko visit the local public health areas in Ivankiv raion in order to monitor adherence to a standard introduction of the study to potential cohort members. (Dr. Tereschenko, who sat in on one of my afternoon sessions with Anna, was to this suggestion.)

② Letter of Introduction to the Project for Entire Cohort

Suggestion: Although it was not possible to get the introduction letter being sent to potential cohort members in English, Anna went through the letter and explained its contents. I was somewhat surprised at its length and rather official nature, but this may in fact be due to the major social and cultural differences between the East and the West. Anna did, however, agree that the letter could be simplified and made more "user friendly," with changes such as simplifying medical terminology, emphasizing that the success of the project is dependent on the participation of cohort members, etc. In addition, I would suggest adding a phrase informing potential cohort members that should they have any questions, they can telephone the Institute of Endocrinology and Metabolism at any time convenient to them.

Anna informed me that only in Ivankiv raion is the letter of introduction from the Ministry of Health being distributed to potential cohort members by local public health personnel, and that in the entire cohort this letter will be sent from the study office.

Suggestion: I did suggest, however, that for cohort members whose addresses are not known at the time of mailing, that any future reliance on local area personnel be closely monitored so that as standard as possible an approach is used for all cohort members. I suggested further that the letter of introduction to the study be changed with emphasis that potential cohort members may inform project staff of periods of time that would be convenient for them (the cohort members) to be examined.

③ Addition of "Postcard" to Introduction Letter:

After some discussion, Anna and I came to an agreement that a postcard be attached to the introductory letter to be filled out by potential cohort members informing the project staff of their acceptance or refusal to be included in the project. Reasons for refusal (such as lack of money, in the Army, in jail, etc.) would be given by potential cohort members so that refusals could be re-approached at a later date with appropriate inducements to become participants. The postcard would also ask for information about other relatives and friends and their addresses, etc., in order for project staff to re-contact potential cohort members who move or become "status unknown" in the future. This profile of relatives/friends will aid in the continued follow-up of the participating cohort members as well. The postcard will also ask cohort members to inform project staff by any means possible of when they are planning to relocate with new addresses, etc.

④ Answering Machine:

I suggested that Anna have an answering machine installed so that if potential cohort members have any questions about the study they can telephone the project office, ***at their convenience***. The answering machine will have a recorded message asking the cohort members the best way for the project staff to contact the cohort members to answer questions, etc. and will advise cohort members that they have the option to inform project staff of their whereabouts by telephone, letter or informing local public health officials so that they can more easily be followed-up.

⑤ Self-Administered Dosimetry Form/Interview Form at Examination:

An English version of the self-administered dosimetry form was not available at the time of our visit. Anna, however, did outline the kinds of information asked and we came up with some suggestions to change the form.

The dosimetric questionnaire administered to participating cohort members at examination was also not available to me.

Suggestions: Evidently, the Ukrainian forms are not identical to those used in Belarus and it was our suggestion that all forms be as identical as possible for cross-comparison purposes. In order to institute some form of quality control of the completion of the form, I suggested, for example, that a question be added to the form asking "Who, besides yourself, helped you fill out this form?" and for what parts of the form.

None of the forms to be completed by potential cohort members seemed to be in English and Anna will send these to me in English so that I can try to simplify them as far as possible and make appropriate clarifications.

⑥ Mobile Teams:

Evidently, four mobile teams will be established to examine children and administer dosimetry questionnaires to parents/children who will not be able to attend centralized clinics.

Suggestion: The letter of introduction to potential cohort members who will be examined by the mobile teams should include information about scheduled visits of the mobile teams to raions so that potential cohort members are made aware of when and where these teams will be located in order to make it as convenient as possible for cohort members to attend.

Suggestion: For cohort members who have informed project staff via the "postcard" (see above) that they have no money to travel to central clinics for examination, another letter should be sent informing the cohort members of the availability of the mobile teams in their local areas giving projected dates and locales. Similar letters to non-respondents could be sent in order to make participation in the project as convenient as possible and entice them to participate.

⑦ Training and Quality Control of Dosimetric Interviewers:

Suggestion: It is essential that all project staff and members of mobile teams who interview cohort members be trained to do so utilizing a standardized training manual. Additionally, actual interviews at central clinics and through mobile teams should be regularly observed by project staff. A sub-

sample of interviewed cohort members should also be re-interviewed in order to compare responses with the original interviews.

⑧ Continued Follow-up of Established Cohort:

Anna and I discussed general ideas for continued follow-up of the cohort in order to ensure, as far as possible, complete follow-up.

Suggestion: The overall approach to follow-up should be one of a "living cohort" which demands continual contact with cohort members. Ideas to accomplish this goal might include:

a) Sending "thank you" letters to participating cohort members thanking them for their participation in the study.
b) Sending reports of the progress of the study to local area medical staff so that they, in turn, could inform cohort members of study progress.
c) Sending informative newsletters to cohort members advising them of study progress.
d) Giving small token gifts to cohort members (especially children) when they are examined.
e) Creating a logo for the study with which cohort members may identify. This logo would then be affixed to all correspondence with cohort members and could be put on coffee mugs, tee shirts, etc. for distribution.

⑨ In Utero Study:

Anna and I spent a little time discussing the plans for establishing the in utero cohort. She explained to me that the Center for Radiation Medicine is working with the Institute of Pediatrics to establish a database of women who were pregnant at the time of the Chernobyl accident. As the in utero study would not be initiated for at least two years, little has been done on this study.

Suggestion: I recommended that more attention be devoted to the planning of this study and that a preliminary questionnaire be developed.

Summary:

Overall, I found Anna to be very enthusiastic about the project and receptive to some of my suggestions. However, she is hampered somewhat by the organizational structure of the project (i.e., the seemingly poor communication between the various study specialty groups. As in Belarus, I would recommend that a coordinating committee be established with one member from each subdivision. The committee would meet regularly so that all project staff can better focus on the overall objectives of the study and be aware of activities in each subdivision.

Dr. Robert J. McConnell
Endocrinology

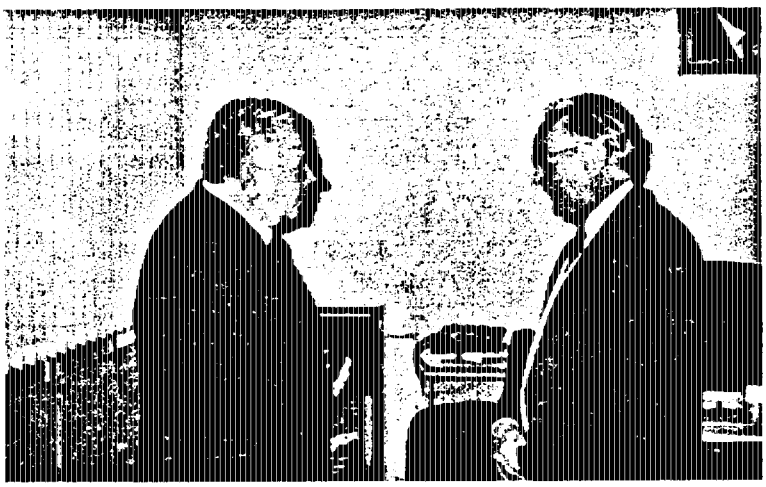
Study of Thyroid Cancer and Other Thyroid Diseases in Ukraine Following the Chernobyl Accident

February 5 - 9, 1998
Kiev, Ukraine

5 February 1998: Arrived in Kyiv this morning after an overnight train trip from Minsk. The accommodations were satisfactory, if not entirely luxurious, and I would not hesitate to do it again. The Hotel Dnipro is well situated downtown, but wildly overpriced.

Institute of Endocrinology and Metabolism

Dr. N. Tronko, the Director of the Institute of Endocrinology and Metabolism, greeted us and then turned the meeting over to his Deputy, Dr. V. P. Tereshchenko. A "plan of activities" is being worked out with the Ministry of Health and they will "soon" be able to finish with the **organizational** phase (unlike the situation in Belarus, the Ukrainians have not begun seeing patients and are hampered by lack of equipment).



Dr. Tronko Greets Dr. Masnyk

The next speaker was the head of the DCC, Mr. V. A. Derzhavets (a.k.a. Slava), who informed us that progress is being made in a "pilot" study carried out in the Ivankiv (a.k.a. Ivankovsky) raion (a.k.a. rayon) of the Kyiv oblast where there has been a 67% retrieval rate. The numbers from the Narodichy (Narodichsky) and Ovruch (Ovruchsky) raions are not as good. Those members of the cohort recorded in the Chornobyl (Chernobyl) Registry are the easiest to find. Dr. V. A. Oliynyk (Deputy Director for clinical work) confirmed that 3 mobile teams will be "ready to go in 2 or 3 weeks." Next up was Dr. O. V. Epshtein, Director the Central Laboratory, who listed his difficulties:(1). Centrifuges, ultrasound equipment, and a calcium analyzer are in his laboratory but under "seal" by customs and cannot be used; (2). He needs a "box" in which to transport the portable ultrasound equipment; (3). He needs vacutainers. He also made the suggestion (not warmly received) that sequential numbers (instead of bar codes) be used to identify laboratory specimens.

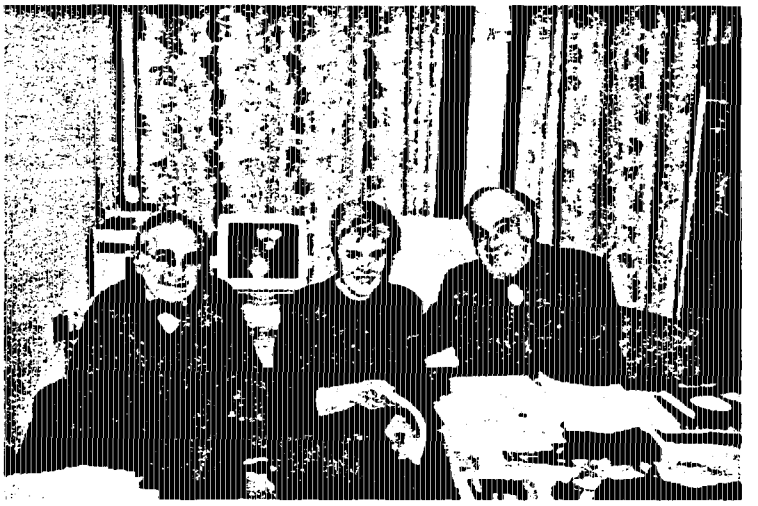
Dr. T. I. Bogdanova, Head of the Morphology (Pathology) Group, has 23 cases of thyroid cancer (21 are from the cohort) and also has information concerning thyroid malignancies since 1987 and abnormal pathology reports dating back to 1968 (when the first of the cohort was born). However, she has only 5 cases of benign pathology (as opposed to the 23 cancers), a point which surprised Dr. Robbins and lead to a sharp retort from Dr. Bogdanova. Her laboratory is "up and running", using equipment, reagents, and supplies donated by the European Union. Although she requests a new computer in order to facilitate data transfers with the DCC, she has been cobbling together her own study in parallel with the DCC on a machine that looks dated, but adequate.

Dr. O. V. Ephstein

Dr. I. A. Likhtaryov, Head of the Dosimetry Group, was not present, so his Deputy spoke in his place. Although they have no problems with equipment, there are "not enough chairs for the American observers." Dr. Markov, the QA officer, admitted that this was a "new area" (I believe that he really meant "new concept") and that he plans to share his responsibilities with the department heads. Then, Dr. A. Derevyanko (Head of the Epidemiology Group) informed us that he has addresses for 495 members of the cohort from the Ivankiv raion and 100 from the Kyiv oblast and will be asking local "authorities" to "assist" in the contact process (by working through the Public Health Service, schools, door-to-door, etc.).

Memo: We all miss Gil Beebe, the "soul" of the project. Somehow I doubt that the mobile teams will be on the road in several weeks.

6 February 1998: Dr. Tronko greeted us, changed the agenda for the day yet again, and introduced Ms Olga A. Bobyljova, the Deputy Minister of Public Health in charge of the operation at Chornobyl, who discussed more "problems": Exposed children have "gown and scattered" and are difficult to locate. The Ministry of Health has enlisted local public health workers (who are looking for funding) and school authorities (about 30% of the cohort are currently of school age) to assist in the search process. After she suggested doubling the cohort size to 40,000, there was a lively discussion of the merits of this approach (although it was likely that this would bias the study in favor of the "responders").



Drs. Robbins, Bogdanova, and Brill

Drs. Robbins, Brill, and I then spent a long and productive day revising the Pathology Form with Dr. Bogdanova. We also had the pleasure of meeting Dr. S. J. Rybakov, from the Department of Surgery, and touring his operating facilities.

Memo: Dr. Bogdanova is talented and enthusiastic, if a little caustic at times, and we should strengthen ties with her and Dr. Rybakov. She is already writing a paper with Dr. Virginia LiVolsi and might be interested in a collaborative study with Dr. E. Greenebaum. Dr. Rybakov expressed interest in a visit by American surgeons and perhaps this could be arranged with Dr. Paul LoGerfo, the chief thyroid surgeon at the Presbyterian Hospital.

7 February 1998: Today we met with Dr. Oliynyk and several of his colleagues, but not Dr. Terekova, who is personally doing the clinical screening. Dr. Robbins and I reviewed a sampling of 14 clinical forms, but this was a frustrating and unrewarding exercise since no English translation was available.

Memo: We need to obtain an English translation of the Clinical Screening Form (it was promised to us, but not delivered- "Slava handles this").

8 February 1998: Had a wonderful tour of Kyiv organized by Dr. Mincey, who has lived there for extended periods of time.

Memo: It is better to "weekend" in Kyiv than in Minsk. The opera is wonderful and inexpensive and the architecture is superb.

9 February 1998: Observed 2 ultrasound-guided FNABs done in Dr. Epshtein's clinic. The patients are screened in the Polyclinic, a separate building, and then referred for the procedure. It is not clear to me what criteria are used for referral of "suspicious" glands,

but the screening Endocrinologist makes the final decision. Dr. Epshtein has the major referral center in the Ukraine and his staff has a lot of experience (they do over 1000 biopsies a year). A 21-g x 1 ½ needle is used and a cytopathology technician screens all of the slides, a very efficient and slick operation. Yet, it is unclear if there is any QA and we did not see a Cytology Form.

Dr. Mincey Addresses the Plenary Session

Back at the plenary session, Mr. Derzhavets promised the group that by the time of the next visit (tentatively set for mid-May) the DCC should be able to have "finished" analysis of data on 20,000 cohort members. Dr. Burch then discussed the establishment of a "living cohort" and Dr. Mincey made the fine suggestion that QA be in place "before screening takes place." Dr. Brill expanded on this point and described the 2 major elements of QA: acceptances testing and project monitoring. When I suggested that these principles be applied to the Pathology Form, Dr. Bogdanova misinterpreted my remarks to mean that she was turning out faulty pathology reports. I also asked her to coordinate the Form with Dr. Cherstvoy in Minsk and urged her to begin using it without delay (she wishes to procrastinate pending the receipt of a new computer, which she says would facilitate "coordination" with the DCC). Dr. Tereshchenko concluded the session by firmly stating that "the next meeting will be a discussion of results." After lunch, Dr. Robbins and I met briefly with Dr. Terekova to discuss the screening process, but there was no time to observe this directly.

Memo: Clinical case conferences might improve QA, but I am not sure that Dr. Oliynyk would be as receptive to new ideas as would Dr. Bogdanova.

Conclusions: This trip was a useful introduction to the personalities, problems, and posturing that will require our attention if this is to be a worthwhile undertaking. Although they appear to have the will to carry out the study, our colleagues in Belarus and the Ukraine lack the money and organizational skills needed to successfully manage a project of this magnitude. I have an idea that progress will continue to be glacial unless we continuously apply the necessary oversight and motivation.

Comrade Lenin

TRIP REPORT: UKRAINE THYROID PROJECT
DATA MANAGEMENT AND ANALYSIS
KIEV, 98.02.05--98.02.09

Daniel F. Heitjan, PhD

Data Coordinating Center

Vyacheslav (Slava) Derzhovets, the head of the DCC, was present each day but was frequently called out to go on purchasing trips. We did have time to visit the DCC and review its operations.

The DCC occupies a large office on the fourth floor of the Institute of Endocrinology. Their computers are older models that cannot run the database software that the project will eventually use. Until new equipment arrives, they are making do. The machines that are not currently dedicated to data management are being used for word processing.

Recruitment of the Cohort

At the plenary session on 5 February, Slava presented a complicated diagram showing the result of efforts to identify the cohort. An initial 20,000 names have been chosen, including 10,000 in the high-dose group and 5,000 each in the lower-dose groups. Of 737 names selected in Ivankov rayon, they found addresses for about 2/3, 351 from the Chernobyl registry and 319 by "manual search" (including some overlap). So far, only a handful of subjects have been screened.

Later in the same session, officials of the Ministry of Public Health made a presentation, the gist of which was that they wanted to increase the size of the cohort by enrolling everybody they could put their hands on. This struck me as a bad idea, as it could introduce a large selection bias.

Biostatistics and Epidemiology

As in Minsk, there appears to be no biostatistical support. Dr. Kairol mentioned that a statistics professor at a local university was supposed to be involved in the project. We suggested that he be invited to future meetings. If he is, as I suspect, primarily a theoretical statistician or probabilist, he may be of little use to the project. In any event, we need to identify an on-site project statistician and give this person the necessary training and resources. We can provide backup and guidance remotely.

The project epidemiologist, Dr. Anna *?*, seems to have little research experience. Fortunately, her English is good enough for fruitful communication.

Data and Forms Quality Control

Several of us spent time trying to review the forms, which had been derived from the Belarus project. Only a Russian version was available, and we struggled with it with the help of Slava and other interpreters. Nevertheless, we managed to identify some potentially significant modifications and some errors that had cropped up in the editing.

The palpation and ultrasound forms contain diagrams of the neck and the thyroid where the examining physicians will mark any lesions that they find. The DCC had set up screens that allow the data entry

person to copy these drawings freehand with a Paint-type program. This will be a time-consuming and error-prone process, and the data will not be usable in a conventional statistical analysis. It makes more sense to simply scan these images in.

Our Ukrainian colleagues had screened a handful of subjects in a pilot study. On Saturday morning, several of us sat with Dr. Oleynik and looked through the data. I had the impression that the person who had conducted these interviews was inexperienced or perhaps had not received adequate training. It was also unclear whether our Ukrainian colleagues themselves had reviewed the data.

Although the number and content of the forms are essentially fixed, the specifics continue to evolve, and of course there may be changes and additions over time. In my experience, minute details of the forms can have a significant impact on the quality of the data, and thus it is essential to review the forms carefully and test them in the field. There should be an interdisciplinary group with responsibility for content and quality, and this group should operate under specific, written procedures for changing and adding forms, and documenting any changes. It was evident that no such process is yet in place.

Planning and Preparation for Joint Meetings

The schedule was a constant source of frustration. It seemed that we and our hosts never had the same idea what would happen next. On a couple of occasions, we agreed in plenary session what site we would tour or what procedure we would observe the next day, but when the time came our hosts would have mysteriously changed the plan.

Translation was a continual problem. I met more English speakers in Kiev than in Minsk, but few were fluent, and we never had the same translator twice in a row. Slava's English is not bad but he lacks confidence and this inhibits conversation. It would be helpful to stabilize the translation situation.

It would also be helpful if our Ukrainian colleagues would prepare better for our meetings. For example, the absence of English translations prevented us from adequately reviewing the forms and the pilot data. And at the final plenary session, we reviewed a list of tasks that seemed to refer to the current, i.e. past, quarter. But on inspection they apparently pertained to the upcoming quarter. In any event, better planning and organization would have made the meetings more fruitful.

Dr. Daniel Fink
Clinical Laboratory Management
and Quality Control

February 5 - 9, 1998
Kiev, Ukraine

The study here is not yet screening patients in significant numbers or generating significant numbers of laboratory results. I met twice with Dr. Epstein and Dr. Mincey to discuss laboratory issues. Amberlite reagents initially had been selected for performing TSH, T4, TPO, TG in the study laboratory although these are not the methods in use in the clinical endocrinology laboratory. However, these reagents are being discontinued and different reagents must be used. Dr. Epstein has a Berthold chemiluminescence system in the laboratory with reagents from the German company Brahms available for all the assays to be used in the study. These reagents have a reputation for quality. Although a little more expensive, these seem to be the best choice for the study as all tests could be done on the same instrument. Dr. Mincey was going to visit Berlin to make arrangements for these reagents after our Kiev visit.

These reagents are not currently used by the laboratory and must be evaluated before use. I discussed with Dr. Epstein how long he thought it would take to set up these tests and he said one day. This would suggest a level of method evaluation less comprehensive than we normally perform in our laboratory. He was unwilling to discuss what steps he would take in setting up and demonstrating the accuracy of these assays.

We also discussed what methods of Quality Assurance Dr. Epstein uses in the laboratory. He monitors his results by freezing specimens and re-testing them on a weekly basis. However, he has no QC material (no money) and does not participate in inter-laboratory comparison programs (they disappeared with the Soviet Union). As in Minsk, we discussed the possibility of exchanging samples and Dr. Epstein was quite interested in this. At the closing meeting, it was also suggested that he could exchange specimens with the Minsk laboratory.

Recommendations:

1. Settle on Brahms reagents and bring them in as soon as possible for full evaluation. I would be willing to assist provide the lab in establishing a standard if Dr. Epstein would be responsive.

2. Quality Control material should be included as reagents in the Brahms reagent purchase so that the lab can begin a QC program. Including QC material with reagents might get them through customs more easily.

3. I offered to exchange specimens with Dr. Epstein's laboratory. He seemed interested in this. I have spoken to FEDEX and they feel that serum specimens on dry ice could be sent directly to Kiev without a problem. They would not be considered a specific biohazard because they are not specifically infectious. Specimens could also be exchanged with Minsk.

4. Data entry mechanism for study data should be tested.

5. Ionized calcium instrument should remain in main lab rather than be moved around. I don't understand the rationale for this and it would require a second machine. I need to discuss this further with Dr. Mincey as he is in favor of this.

6. Reviewed data forms with Dr. Heitjan. They should be finalized and tested.

7. Proper use and centrifugation of serum separator tubes should be verified.

8. Except when the diabetologist was present, translation was a problem. Better interpretation would be an asset.

9. Dr. Epstein's laboratory seems quite proficient but for a variety of reasons, is not performing all the quality management procedures that could be used.

10. I am not sure how amenable to suggestions Dr. Epstein will be.

11. I need to find out if he is going to keep study specimens separate from clinical specimens.

12. A formal procedure for comparing cytology to pathology should be established. It seems like this occurs on an ad hoc basis in an informal fashion.

PART C

Kiev, Ukraine, February 10-12, 1998

Study of Leukemia and Other Hematological Diseases Among Clean-Up Workers in Ukraine Following the Chernobyl Accident

Trip reports for:

- Professor J. David Burch, Epidemiology and Fieldwork
- Dr. Robert Reiss, Hematology and Pathology
- Dr. Edward Haskell, EPR of Tooth Enamel
- Dr. Charles Geard, Biological Dosimetry

J. DAVID BURCH, EPIDEMIOLOGY AND FIELDWORK
February 10-12, 1998, Kiev, Ukraine

Study of Leukemia and Other Hematological Diseases Among Clean-Up Workers in Ukraine Following the Chernobyl Accident

Plenary Session, February 10, 1998
Research Center for Radiation Medicine, Academy of Medical Sciences of Ukraine

The plenary session was chaired by Dr. A. Romanyenko, Project Director. Progress to date for each aspect of the study was described by the Ukrainian investigators. The details of progress to date are included in the current progress report which was supplied to us at the meeting.

Meetings with Dr. N. Gudzenko, Head of Epidemiology Group:

Dr. Gudzenko (Natalia) and I initially discussed the progress to date on the overall project and in pilot phase (Phase 1) of the project. The study will include male clean-up workers only who lived at the time of the accident in five oblasts and the City of Kiev from 1986 to 1990 or at the time of their registration in the Ukrainian National State Registry. The catchment area for potential members is comprised of approximately 97,000 registered clean-up workers. Phase 1 of the project is a pilot phase to determine the feasibility of procedures for identification of the cohort and follow-up. The Oblast of Dnipropetivsk has been chosen to field test procedures.

Natalia brought up a number of questions that have not as yet been answered.

① What are criteria for inclusion in the subcohort?

② Determine if clean-up workers who move out of the catchment area will be included in the cohort.

③ Determine if clean-up workers who were in the military, fire brigade and those employed at the Chernobyl plant at the time of the accident will be included in the cohort.

Pilot work in Dnipropetivsk Oblast will involve the tracing, physical examination and interviewing of a yet undetermined number of members of the subcohort.

Natalia and I subsequently discussed the details of procedures for inviting liquidators to participate in the study and both active and passive follow-up.

Introductory Letter to Potential Cohort Members:

At the time of my meetings with Natalia, there did not appear to be an English translation of the introductory letter. We did, however, discuss ideas for inclusion in the letter.

① The letter should be as "user friendly" as possible, with non-complicated terminology.

② The letter should include a statement about how valuable it is to the project that each liquidator participate in the project.

③ The letter should ask the liquidators to inform project staff about any plans they have for relocation giving new addresses.

④ The letter should include a statement to the effect that the liquidator is invited to telephone, at his convenience, the project office with any questions he may have regarding participation in the project.

⑤ The inclusion of (4 above) will necessitate the project office obtaining an answering machine so that liquidators can contact study personnel at the formers' convenience.

Active Follow-Up:

① For liquidators who do not show up for their annual medical examinations, initiate involvement of local health nurses to maintain contact with these liquidators.

② Send thank you letters to liquidators who do agree to participate in the study reminding them to advise the project office of any plans they may have for relocating with details of new addresses.

③ The thank you letters could also ask the liquidators to specify whom to notify in the case of emergency, i.e., close relatives and/or friends who then would be able to locate the liquidators in case they become lost to follow-up.

④ Newsletters outlining progress in the study could be sent to participating liquidators to help ensure follow-up.

Passive Follow-Up:

① For liquidators whose current addresses are not known, initiate contact with the Ministry of Internal Affairs (Passport Office) to aid in determining addresses.

② Other agencies which could possibly be approached to determine current addresses could include social benefit and certification of victims offices.

Interviewing Procedures:

Natalia and I discussed interviewing procedures and I suggested that the plan to possibly employ medical doctors, a mathematician and/or a former liquidator, may lead to interviewer bias.

We discussed a number of issues regarding interviewing procedures and came up with a number of suggestions:

① In the pilot work in Dniproptivsk Oblast administer questionnaires to respondents both at polyclinics and in liquidators' homes to get a feel for which environment is more suitable.

② The questionnaire could be pre-tested in Dniproptivsk Oblast to determine any problems with its administration.

③ Evidently, there was a workshop in Kiev in April 1997 with possible interviewers from Ukraine, Belarus and Russia for interviewer training, with pre-testing of the questionnaire on 15 liquidators attending polyclinics in Kiev. On the basis of this, the questionnaire was changed to some extent. It is essential that any new prospective interviewers be trained using a standard interviewers' manual and I suggested that since the final questionnaire may be quite different from the original questionnaire used in interviewer training, that ***all*** interviewers undergo training once again.

④ Continual monitoring of interviewing procedures was discussed with the need to observe actual interviews of liquidators to ensure that interviewing follows the standardized approach to cohort members and all questions are asked in the same way by all interviewers.

⑤ I suggested to Natalia that I would look at the current version of the questionnaire and make changes where appropriate, and she agreed. This includes any possible changes to the letter of introduction, asking liquidators to participate in the study.

Overall Impressions:

Overall, I found Natalia to be quite knowledgeable about the study procedures, but as in the thyroid studies in Belarus and Ukraine, hampered somewhat by the seeming lack of communication between subdivisions of the study. Therefore, I would strongly recommend that a coordinating committee with one member from each subdivision in the study be established and meet regularly informing their colleagues of activities and progress in other subdivisions so that the entire project staff can better focus on the overall objectives of the study.

College of Physicians & Surgeons of Columbia University | *New York, N.Y. 10032*

DEPARTMENT OF PATHOLOGY DR. ROBERT REISS, HEMATOLOGY AND PATHOLOGY 630 West 168th Street

March 10, 1998

Geoffry R. Howe, Ph.D.
Professor and Director
Division of Epidemiology
Columbia School of Public Health

Dear Dr. Howe:

As promised, I am writing a review of my impressions of the meetings held with the Ukranian members of the Leukemia / Lymphoma study group during my trip to Kiev from February 9 to 12, 1998. In particular, I would like to describe the activities of the working group of hematologists with whom I interacted. Aside from myself, this group consisted of Drs. Finch, Klimenko, and Dyagil. Dr. Babeshko was not present for any of these meetings. In addition, he was not present for any of the larger meetings held by Drs. Romanenko and Masnyk.

Our meetings were cordial and business-like. Communication was limited by the fact that Dr. Klimenko speaks no English and Dr. Dyagil has only moderate ability. They obviously have a great deal of respect for Dr. Finch, but also seemed to be interested in my points of view. Unfortunately, they seemed to be even more interested in their points of view which were heavily weighted toward the utilization of advanced technology, whether it be appropriate or not.

Inspite of the number of hours during which I interacted with Drs. Klimenko and Dyagil in rather intense working conferences, I have not formed a clear idea regarding their diagnostic and clinica skills. Of concern, however, was the fact that I got the distinct impression that they wished to exclude participation of the pathologists from the Oncology Institute in the study while not possessing any minimal expertise in lymphoma tissue diagnosis themselves. It is not clear what they propose to do, but I fear they may even try to train one of their clinicians to fulfill this role. Furthermore, although agreeing to a pathologic classification that does not make use of immunologic markers, they insist on the need to utilize such immunologic reagents in the laboratory and repeatedly stated that the above mentioned clinician can also be trained appropriately to utilize such technology.

The laboratory facilities are likewise marginal and there are no pathology facilities on site. They may be planning to ask the Oncology Institute to prepare paraffin blocked tissue slides and possibly even frozen sections for them. I would be most suprised if the Institute would allow itself to be used in this way, since they would be excluded from taking responsibility for pathologic interpretation of these tissues. All in all, I think that such a plan is unworkable. Although they do have a flow cytometer, I was unable to get a good grasp on its capabilities. Full utilization of the

FAB classification of the leukemia is dependent on this technology. Perhaps Dr. Matshushima needs to be consulted. In an attempt to bring some order to these plans and proposals, I promised to try and develop guidelines for the use of surface marker identification in the diagnosis of leukemias and lymphomas. I will be meeting with Dr. Matshushima to work on this.

Their plans for sample storage are grossly oversimplified. Currently, they have no system in place to maintain an inventory which can be accessed to find a specific sample. Once the freezers are obtained, we will have to work closely with them to develop a suitable inventory system.

It appeared that Dr. Romanenko's next priority is to meet again in May and to travel to Dnepropetrovsk in order to directly encourage that regional participation. It was unclear how much of the hematologic nuts and bolts of the leukemia project would be reviewed with local physicians and hematologists. None the less, Drs Klimenko and Dyagil repeatedly asked that I be included in the group. Unless there is to be further discussion of the classification of leukemias and lymphomas or of laboratory protocols, I am not sure I would really be needed. I already have informed your office that I will be away from May 11-May 17.

In summary, I found the meetings interesting but somewhat disturbing. I will be curious to see what happens next. I would also be very interested in the impressions of the leukemia group epidemiologists and dosimetry experts. Will you be holding a review meeting for all of us this spring?

Sincerely,

Robert F. Reiss, M.D.

Summary Trip Report of Dr. Edwin Haskell to The Ukrainian Scientific Center for Radiation Medicine as Part Of an NCI-Sponsored Study On Leukemia And Thyroid Cancers Associated with the Chernobyl Accident.

February 8 to 13, 1998

Monday 2/9/98

Meeting with Vadim Chumak and Sergei Sholom at USCRM EPR Laboratory, Kiev.

We reviewed the summary of recent work performed at the Center for Applied Dosimetry at the University of Utah in conjunction with the visit of Dr. Alex Romanyuhka from the Institute of Metal Physics, Ekaterinburg, Russia. (Report included in Appendix 1) The work centered on analysis of Russian teeth, many with extensive caries, and was designed to produce dose estimates on low dose background teeth from regions near the Techa River. The method of analysis was similar to that in use at the USCRM. We observed discrepant results and through follow-up work discovered significant errors were being introduced due to 1) distortion of the native signal, 2) changes in sensitivity to radiation induced by diseased (caries) teeth and 3) induction of a signal overlapping the dosimetric signal of enamel . In addition we observed virtual elimination of the native signal in enamel subjected to extended treatment in KOH in an ultrasonic bath. Drs. Chumak and Sholom indicated that tests had been made in their laboratory to rule out such possibilities and raw data was produced by them for examination. Upon examination of the spectra of enamel which had been subjected to prolonged treatment in KOH, it became obvious that a consistent signal was being induced near to the location of the dosimetric signal. As with the Utah results, the signal was not in the exact location of the dosimetric signal but was near enough to introduce a systematic error in dose estimation. Dr. Sholom stressed that they had not seen reduction in the native signal of enamel with prolonged treatment in KOH and offered to provide enamel grains which had undergone 3 months treatment in KOH (in a study designed to examine loss of mass with treatment time) as proof. Dr. Sholom had not examined the spectra from these samples and I suggested we examine them immediately on his spectrometer. The results were in agreement with our results since according to Dr. Sholom, the spectra produced had a native signal approximately half the intensity of the lowest amplitude signal which had ever been recorded at the USCRM. At that point it was agreed that the other findings at the U of Utah should be replicated during the pending visit of Dr. Sholom to the University of Utah laboratory. The protocol for the visit is included in the Appendix. We discussed one area of sample documentation which could effect interpretation of results, should disease be shown to introduce systematic errors. That was the lack of in house documentation of condition of each tooth sample. At present the only information being entered into the database is the reason for extraction supplied by the dentist. I suggested that a close-up photograph of each tooth should be

made prior to sample preparation as is done at the University of Utah. Such a photograph could then be referenced at a later date and the results modified or excluded based upon yet to be determined visual criteria. An example photograph of a tooth which displayed a factor of 6 lower sensitivity than normal is shown in the Appendix. The equipment that I recommended for the photographic documentation included: 1) Nikon N70 SLR camera, 2) Nikkor 55mm macro lens, 3) Nikon SB23 electronic flash, 4) Nikon SC26 remote flash cable. The total price of the above equipment would be under $1000.

Tuesday, 2/10/98

Meeting of U.S., French and Ukrainian participants at USCRM headquarters.

Dr. Romanyenko presided over a general meeting of project participants. Each aspect of the project was described by the Ukrainian investigators and the descriptions were largely as described in the current progress report. Those descriptions will not be included in this report. An issue which surfaced repeatedly included logistical problems with customs, shipping and documentation. Precise documentation is required before duty-free customs clearance can be granted, and the documentation has not been consistently included in the shipments up to this time. Time-critical supplies could easily go bad in the time required for customs clearance. On this point I would offer the suggestion that in the event that paperwork on time sensitive shipments has not been adequately prepared, consideration be given to paying the required duties to release a shipment from customs. This could be a far cheaper solution than ultimately taking delivery of outdated chemicals and having to reorder (and repay) for a new shipment.

Concerning the report of Dr. Chumak concerning EPR dosimetry of teeth and identification of affiliation of liquidators, Dr. Chumak summarized the discussion which we had had the previous day (see above), described results of the questionnaire sent out (see below) and presented plans for quarter 2 which included a visit by Dr. Sholom to the University of Utah (see appendix) as well as set up and testing of the EPR equipment due to arrive during the quarter. He briefly mentioned protocols for the intercomparison of EPR, FISH, registry doses and analytical reconstruction. This topic was discussed further with the dosimetry group on Wednesday.

Dr. Phillipe Hubert described his attempts at a recent Moscow dosimetry meeting to solicit support for open sharing of all data by the various organizations and countries involved in Chernobyl dose reconstruction. His proposal was suggestion was not accepted.

Following lunch, the dosimetry group toured the clinical diagnostic facilities of the Polyclinic and computing facilities of the State Registry.

Wednesday, 2/11/98

On Wednesday members of the dosimetry group, including Phillipe Hubert, Paul Vollique, Charles Geard and Ed Haskell, visited the EPR laboratory for discussion of dosimetry related topics and review of protocols for intercomparison of FISH, EPR, analytically reconstructed doses and doses from the national registry.

Pilot questionnaire study.

Dr. Chumak first described the pilot project which he was conducting to assess ability to locate registry entrants on the basis of their addresses in the state registry and to assign affiliation at the time of cleanup. Affiliation is not indicated in the state registry and is an important criterion for assigning doses to groups of individuals on the basis of their types of activities during cleanup. The study involved the mailing of questionnaire postcards to approximately 3700 individuals in a single Blast who met the following criteria. 1) they must have had their dose recorded in the state registry, 2) they must have been liquidators between the years of 1986 and 1987, and they must have had an address of residence at the time of registry entry in the Blast being studied. Questions on the post cards were explained to the group and changes which would be made to several of the questions before a full scale mailing were described by Dr. Chumak. Over 1,000 post cards had been returned and another handful arrived the day we visited. Several possibilities for locating liquidators who were missing from the registry were also discussed. Dr. Chumak explained that the local polyclinics had a data card for each patient treated at the clinic. The card had a field for the local ID number of the patient (unique to the clinic), a field for the state registry number of the individual, if any, and a field indicating if the individual was classified as a liquidator. It would be possible in theory to check the cards at the polyclinics (much of the data is in electronic form) and flag those cases where the liquidator status is indicated, but a state registry number is not entered. Another possibility is to check databases of local authorities who confer liquidator status and match entries against names in the state registry. To obtain liquidator status an individual must present 1) military certification as a liquidator, 2) travel certificates indicating travel to and from the cleanup site, 3) accounting records indicating payment as a liquidator or 4) copies from the archives of the Ministry of Defense.

Description of EPR databases

Dr. Chumak described and demonstrated the databases associated with liquidator tooth specimens, including aspects of sample preparation, treatment method, quantity recovered, quantity measured and amount remaining for further examination. Another database was demonstrated which contained raw and compiled data related to EPR measurements. This database provided access to individual spectra, processed spectra (where empty cavity measurements had been subtracted and spectra normalized for field position), doses applied to the samples, and plots of the dose response curves for each sample.

It was agreed that the first criteria of such a study should be the availability of teeth from liquidators appearing in the registry. Although this seems obvious given the low level of availability of teeth from liquidators, there had been suggestions on the part of the hematology group that subjects should be selected from those displaying hematological abnormalities likely associated with radiation exposure.

Protocol for Working Visit of Dr. Sergei Sholom to University of Utah

We propose a working visit of Dr. Sergei Sholom to the University of Utah to verify the effects described in the attached document and to determine the magnitude of the effects on dose estimation using the sample preparation procedures in use at the EPR Laboratory of the USCRM.

The investigation would fall into two broad categories. Quantification of those effects which have been seen at the USCRM, and verification and possible quantification of those effects which have not been observed.

The first category includes the reduction in size of the native signal of enamel with extended treatment in KOH as well as the addition of a signal during chemical treatment.

The second category involves the location of the induced signal. The USCRM has identified an added signal with an offset of the g-factor relative to the dosimetric signal. The exact location of the signal, its rate of induction with KOH treatment, and its effect on dose measurement should be investigated. The other area which has not been confirmed by the USCRM is the change in sensitivity induced by prolonged KOH treatment. This effect will be investigated in several Ukrainian samples by preparing and measuring one half of each tooth at the University Utah using methods previously shown to induce sensitivity changes. The other half of each tooth will be prepared and measured on return using routine methodology of the USCRM. A third effect not seen at the USCRM is the change in sensitivity of the dose response curve of teeth as a function of dental caries. This will be examined by collecting up to 15 teeth with dental caries and 15 teeth without dental caries. The dose response curves for these teeth will be constructed and analyzed at the University of Utah. A portion of those teeth of sufficient mass will also be prepared such that areas of enamel at increasing distance from the location of the caries will be separately collected. It will then be possible not only to examine the range of the sensitivity change between teeth (if any) but also the range of the effect with distance from the active caries sight. Another factor concerning sensitivity changes associated with dental caries is the effectiveness of chemical preparation in removal of effected pre-carious enamel. The influence of grain size on treatment efficacy will also be examined. It is anticipated that the full investigation of these issues will not be completed during the two month visit of Dr. Sholom and it is suggested that the investigations be continued and completed at the University of Utah following his departure.

Effects of Caries and Sample Preparation Procedures on Accuracy of EPR Dose Measurements: Preliminary Results

A. Romanyuhka, E. Haskell, R. Hayes and G. Kenner

In October, 1997, Dr. Alex Romanyuhka began a working visit to the University of Utah with the aim of 1) evaluating and gaining proficiency in the routine EPR procedure in us at the Utah laboratory and 2) measuring background dose in several dozen teeth obtained from potential background regions (Chelyabinsk and Kurgun Oblasts) in the South Urals between 50 and 100km from the Techa River. During this visit we discovered variations in the EPR measurement of radiation doses in background teeth from the Urals region of Russia beyond those expected from our previous experience. Closer examination revealed differences in the shape of the "native" signal of the Urals teeth relative to that of the standard background spectrum in use at the University of Utah for subtraction of the native signal during spectral analysis. It appeared that small variations in the shape of the native signals were causing errors in the dose estimations of up to several hundred mGy. We were also using a sensitivity standard appropriate for healthy U.S. teeth, but assumed that the accepted sensitivity variations between teeth of 10 to 15% would not be a major source of error .

We had used KOH with ultrasonic treatment for preparation of the Urals teeth (in a manner similar to that used by the Ukrainian Research Center for Radiation Medicine in Kiev), while our native background standard had been prepared using NaOH with ultrasonic treatment (the usual procedure at the University of Utah). It was impossible, therefore, to immediately identify the source of our errors as being the teeth, their less than healthy state, the sample preparation treatment, the sensitivity standard or some combination thereof. Although our immediate problem was largely rectified by development and application of a new background signal and measurement of individual sensitivities for each tooth examined, we felt that the variations we had observed required closer examination.

We broadened our research program from routine dose estimation of the 36 background teeth to an examination of variations in the sensitivities of the teeth, the magnitude of the spectral differences of the native signals, the effects on dose estimation and the sources of the spectral and sensitivity variations. We should point out that the Inco Copurnicus EPR program of the European Union had attempted to address the question of variation due to sample preparation and had not uncovered the types of problems which we were now observing. This was likely due to several factors; 1) we were not analyzing entirely healthy teeth, 2) analyses were now being made on a single spectrometer making direct spectral comparisons feasible, and 3) greater precision was possible using instrumentation and methodology for removal of sample anisotropies and dynamic instrumental variations. The latter improved reproducibilities by an order of magnitude allowing detailed examination of small spectral variations.

Our research program was designed to address the sample preparation methods currently in use by major laboratories: No treatment, Obninsk; KOH with ultrasound at 60°C, Kiev; NaOH with ultrasound at 60°C, Utah. It was assumed that any effects induced by NaOH treatments with ultrasound at approximately 40°C as done at GSF and Ekaterinburg would be revealed by treatment at the higher temperature of 60°C used here.

Research Program:

1) Comparison of changes (spectral and sensitivity) induced by chemical treatment.

Methods were compared by treating separate portions of the same tooth in NaOH and KOH for varying periods of time. Results were compared against untreated portions.

2) Comparison of spectral parameters and sensitivities of healthy versus diseased (caries) teeth.
3) Relative effects of chemical treatments on healthy versus diseased teeth.

Summary of Results:

1) KOH has a more rapid and pronounced effect on "cleaning up" the enamel spectrum than does NaOH. This spectral cleaning is critical to spectral reproducibility at low doses.
2) KOH treatment can reduce and even eliminate the native signal. Removal of the native signal has long been thought to be one means of improving measurement accuracy.
3) KOH treatment induces a signal at radiation measurement locations equivalent to approximately 300mGy over a 70 hour period.
4) 70 hour KOH treatment causes an increase in sensitivity to radiation of approximately 15%.
5) NaOH treatment induces a signal at the radiogenic signal's location equivalent to approximately 20mGy per hour of treatment.
6) The above effects are exaggerated when teeth with caries are treated.
7) The native signal is broadened in teeth with caries.
8) This effect extends beyond the region of visible disease into apparently healthy portions of the tooth.
9) Teeth with caries have a lower sensitivity to added radiation. One tooth examined had its sensitivity reduced by a factor of 6.
10) Approximately 10% of the Urals teeth examined were unsuitable for analysis due to high caries content.

Conclusions and recommendations

1) The dosimetric effects of teeth with caries can be large. The effects extend beyond the visibly diseased regions.
2) At the present time, measurements of teeth with extensive caries should not be used for dosimetry purposes. Teeth with caries from the exposed Mayak and Techa river populations should be archived until methods are developed for the analysis of such samples.
3) Effects of tooth preservative methods (70% ETOH, 10% formaldehyde, etc) should be evaluated
4) The extent to which the pre-carious portion of a tooth exhibits altered dosimetry properties should be examined. It may be possible to develop spectral screening procedures to identify pre-carious alterations by identifying spectral broadening (observed in this study) during analysis. This would be useful for pre-caries teeth with little or no visual indication of disease which may slip by a preliminary screening process.
5) Systematic uncertainties due to sensitivity change and increase in radiation signal size may be introduced by the use of KOH and NaOH treatment. This effect should be examined further to determine the magnitude of the effect in a number of healthy and diseased teeth, and an optimal cleaning regime with minimal artifact introduction should be developed.
6) Given that EPR dosimetry on tooth enamel is in a rapid state of development, non destructive methods should be used whenever possible so that samples can be reanalyzed as the technology advances. Development of a procedure allowing

nondestructive measurements with correction for tooth to tooth sensitivity differences was recently proposed to EH-63. (see attachment).

7) The use of non-destructive methods with a standard EPR sensitivity curve can produce large errors in teeth with caries. Non destructive methods must take into account individual sensitivities, alternatively, the uncertainties associated with those measurements should be more realistic estimated.
8) All existing methods of spectral analysis should be examined and those most suitable for handling native signal variations should be compared for speed and accuracy of analysis.

92 1925 60

Dr. Charles Geard
Biological Dosimetry

Hotel Dnipro
5pm Sunday 8th February
Introductory get-together of Columbia-NCI groups including those participating in the Belarus thyroid study. Discussion of meetings and assignments for the week.
Comment: It would have been far preferable if most of the information outlined had been made available in the U.S.

Monday 9th February am
Visited Dr. Maria Pilinskaya with Dr. Stuart Finch. Dr. Pilinskaya is an established radiation cytogeneticist who is tasked with undertaking biological dosimetry on liquidators using chromosomal changes as indicators of dose. This latter will be established using whole chromosome painting probes and fluorescent in situ hybridisation (FISH) technology.

Dr. Pilinskaya indicated deep frustration with the lack of supplies and equipment. She stated that she had no phytohemagglutinin for stimulating human lymphocytes, no growth medium and inadequate microscopic equipment to undertake FISH analyses.

It should be noted that Dr. Pilinskaya was recovering from surgery and this meeting took place in her apartment.

Dr. Finch attempted to define the organisation and hierarchy of studies and of those involved with Dr. Pilinskaya with partial success.

Dr. Pilinskaya also indicated that due to lack of refrigerator space she was storing biological samples in the refrigerator of her apartment.

Comment: In the absence of an assessment of the laboratory and its equipment, I can make no judgement on the practical aspects of this important component of biodosimetry. I noted however that Dr. Chumak was the individual tasked with selecting those persons to be sampled for chromosomal studies. Hopefully, this could be aligned with the initial

studies which used chromosomal biodosimetry to indicate doses as high as 13 Gy in liquidators.

Monday 9th February
Accompanied Drs. Finch and Reiss to the Hematology Clinic. Reasonably impressed but I leave medical judgements to Drs. Reiss and Finch. I was not persuaded however as to the utility of undertaking chromosomal studies at this time. They would only be really informative in a sub-set of individuals.

Tuesday 10th February
Plenary session
Interesting, but in the absence of adequate pre-visit or of pre-meeting information dissemination relatively confusing.

Wednesday 11th February
Visited the laboratory of Dr. Vadim Chumak, Head of the Laboratory of External Exposure Dosimetry Department of Dosimetry and Radiation Hygiene.
Dose assessments using electron spin resonance (ESR) dosimetry from tooth enamel. A large well organised and co-ordinated laboratory with an established mechanism for identifying and collecting teeth extracted from liquidators. Use of ESR for dose-estimation is also an integral part of the cataract study (Dr. Worgul).

Comment: This approach relies on extracted teeth. Chromosomal biodosimetry relies on relatively small blood samples. Since a close correlation between ESR dosimetry from tooth enamel and cytogenetic dosimetery from lymphocytes of Hiroshima atomic bomb survivors has been established (I.J.R.B. in press) it is very important that the dosimetry programs be organised such that information optimisation results.

Thursday 12th February

Plenary session
Documents submitted, discussed and presumably finalised. In terms of tasks completed, a fairly comprehensive documentation with variable meaning.

Overall: Prospects are good for the likelihood of obtaining meaningful risk estimates for cancer induction in a human population following radiation exposure. The phased approach appears to be working.

I would however note the biological dosimetry component as being behind the other dosimetry components. This situation should be alleviated by the provision of appropriate supplies and equipment as expeditiously as possible. Close monitoring is desirable.

APPENDIX 3

Questionnaire

Leukemia Study Amongst Liquidators in Ukraine

Liquidator's identification # /_/_/_/_/

Research study on the liquidators' state of health

Questionnaire

1997-2000

Moscow, Minsk, Kiev, Obninisk,
Lyon, Washington

The following organizations and institutes have participated in creating of this questionnaire:

Belarus
- Belarusian Center of Medical Information Technologies of Management and Economy of Public Health (Minsk)
- Institute for Scientific Research on Hematology and Blood Transfusion (Minsk)
- Institute of Oncology (Minsk)
- State Center of Oncopathology of Thyroid (Minsk)
- Institute for Scientific Research on Radiation Medicine (Minsk)

Russia
- Medical Radiological Scientific Center (Obninsk)
- Institute of Biophysics (Moscow)
- Military Medical Academy (St. Petersburg)

Ukraine
- Chernobyl Nuclear Power Station (Chernobyl)
- Scientific Center of Radiation Medicine (Kiev)

European Commonwealth
- European Commission (Brussels, Belgium)
- International Agency for Cancer Research (Lyon, France)
- Institute of Nuclear Defense and Security (Fontane, France)

USA
- National Cancer Institute (Washington)
- Columbia University (New York)

Information on a liquidator from the Chernobyl Registry

	Chernobyl Registry	Corrections, if any
0.1 Last name	_____	_____
0.2 First name	_____	_____
0.3 Patronymic(middle name)	_____	_____

0.4 Date of birth day/_/_/month/_/_/19/_/_/

0.5 Identification document (pictured I.D.):

1. passport
2. military registration card
3. other, please specify_____

_____

I.D. code _____ _____

I.D. # /_/_/_/_/_/_/_/_/_/_/_/_/

0.6 Home address

postal index /_/_/_/_/_/_/

oblast (district) _____

region _____

if you live in a city:

city (name)_____

street _____

house # /_/_/_/_/

apartment # /_/_/_/_/

if you live in a village:

village council (local authority) _____

type of village (depending on the number of population, it may have different names)_____

0.7 telephone #: work /_/_/_/_/_/_/_/_/_/_/

home/_/_/_/_/_/_/_/_/_/_/

Last name, first name, patronymic (middle) of the interviewer_____

Date of the interview: day/_/_/ month/_/_/ year 19/_/_/

The interview began at: hour/_/_/ minutes/_/_/

The person being questioned is:

1 ☐ liquidator
2 ☐ his wife
3 ☐ his brother or sister
4 ☐ his daughter or son
5 ☐ other, specify

If the person who was questioned, is not a liquidator, put his/her last name, fist name and patronymic down _____
and also put down the reason why the liquidator himself was not been able to answer the questions:

1 ☐ died
2 ☐ too sick to answer questions
3 ☐ is on an extended business trip
4 ☐ other, specify_____

Do you know names and addresses of colleagues of your husband (brother, father,...), who worked with him in the area of the Chernobyl power station. If yes, please put them down:

Last name, first name, patronymic	Address, telephone #
_____	_____
_____	_____
_____	_____
_____	_____

1. General data on the liquidator

At first, I would like to ask you a few general questions and then to ask you to present your documents confirming that you are a liquidator.

1.1 Your nationality (choose one option)?

1 ☐ Belarusian 3 ☐ Ukrainian
2 ☐ Russian 4 ☐ other, specify_____

1.2 Your marital status (choose one option)?

1 ☐ married (that includes living together) 3 ☐ widower
2 ☐ single 4 ☐ divorced

1.3 What kind of education did you have (choose one option)?

1 ☐ hasn't finished high school 3 ☐ certificate training
2 ☐ high school 4 ☐ college

1.4 Please, show me the document which confirms that you are a liquidator.

a. If the document is presented, the following information needs to be put down:

Type of the document	Code, # and the date of issue	Organization which issued the document
_____	/_/_/_/_/_/_/_/_/_/_/_/_/ 19/_/_/	_____

b. If there is no document (lost, etc.), please, tell me (if the liquidator forgot, put down "doesn't remember"):

the reason, why he doesn't have the document_____
type of the document_____
the organization which issued the document_____

1.5 How many times were you sent to the 30 kilometers zone (choose one option)?

1 ☐ once 3 ☐ three times
2 ☐ two times 4 ☐ more, specify_____

Parts 2-4 should be filled out separately for every participation of the liquidator in the work within the 30 kilometers zone. Having filled out parts 2-4 for the first participation, fill out these parts the same way on separate sheets of paper for all other participations in case the liquidator has gone to the zone a few times. If the liquidator doesn't remember the dates you are questioning him about, put 99 for the "year" option (if he doesn't remember the year), and also, put 99 for the "month" option (if he doesn't remember the month). If the liquidator doesn't remember the exact day, ask him whether it happened in the beginning of the month, in the middle or in the end, and put down "n"-if it's the beginning of the month (Russian word for "beginning" starts with a "n"), put "s" - if it's the middle (Russian word for "middle" starts with a "s"), and put "k" for the end of the month (Russian word for "end" starts with a "k").

2. Information about the first participation in the activities at the 30 kilometers zone.

Now I am going to ask you a few questions regarding the reasons of your participating in the activities at the 30 kilometers zone and I will ask you to show me your documents (if you have them) which could confirm the time you claim to have spent in the zone. If you were there a few times, try to remember all your participations and to describe work conditions in the zone, and also living conditions outside of the 30 kilometers zone.

2.1 Please tell me which organization sent you to the 30 kilometers zone (choose one option)?

1 ☐ Army
2 ☐ military committee
3 ☐ organization of the Ministry of atomic industry (including power stations)
4 ☐ Ministry of Internal Affairs/KGB (Committee of State Security)

2.2 Please tell me the full name of that organization during the time when you were sent to the 30 kilometers zone and its location:

name_____
oblast (district)_____
city/other_____
If changed, give the new name_____

2.3 Please tell me the date when you started to work there /_/_/ /_/_/ 19/_/_

2.4 Please tell me the date when your job was over /_/_/ /_/_/ 19/_/_/

2.5 Do you have any official documents which could confirm the time you stayed in the 30 kilometers zone (choose one option)?

1 ☐ yes
2 ☐ no

If yes, please show me the documents.

If there are documents, the following information needs to be put down

Type of the document	Time period during which the person stayed in the 30 km zone of Chernobyl PS
_____	from/_/_/ /_/_/ 19/_/_/ to /_/_/ /_/_/ 19/_/_/
_____	same as above
_____	same as above

2.6 Please tell me the name of the organization you were with during the time you worked at the 30 kilometers zone (only if you haven't done that already).

2.7 Could you show me the official documents regarding the dosage of radiation you received(choose one option)?

1 ☐ yes
2 ☐ no

If "no", please specify the reason why you don't have any documents regarding the above matter:

1 ☐ lost
2 ☐ left at home
3 ☐ other, specify_____

If "yes", please show the documents(*If the documents were shown or the liquidator didn't show them but remembers having them, then it is necessary to put down the following information*):

Type of the document, organization	Code, # and date of issue	Time period, dosage and unit of measurement	Is this a total dosage?
_____	/_/_/_/_/_/_/_/_/_/_/ _/_/ 19/_/	from /_/_/_/_/_/19/ to/_/_/_/19/_/_/	1☐ yes 2☐ no 3☐ I don't know

2.8 Did you work shifts (choose one option)?

1 ☐ yes
2 ☐ no
3 ☐ yes and no, specify the dates of working shifts from /_/_/ /_/_/19/_ to /_/_/ /_/_/19/_/_/
9 ☐ I don't know

2.9 Please, tell me where did you usually work in the 30 kilometers zone and specify how much time (in percents) you worked in these conditions (choose all the options that apply)

1 ☐ outside the houses and transportation vehicles (in open air)
  1 ☐ if yes, specify how much time_____%
  2 ☐ no
  9 ☐ I don't remember
2 ☐ inside a house
  1 ☐ if yes, specify how much time_____%
  2 ☐ no
  9 ☐ I don't remember
3 ☐ in a transportation vehicle (for example, in automobile)
  1 ☐ if yes, specify how much time_____%
  2 ☐ no
  9 ☐ I don't remember
4 ☐ other, specify_____
  1 ☐ if yes, specify how much time_____%
  2 ☐ no
  9 ☐ I don't remember where I worked

2.10 Using the list of the localities, please name main areas where you worked and also the following information (*the interviewer should put down all the main areas-towns, villages-one by one, one per line*).

Area, region	Start date of work d/m/y	Duration (in days)	Average number of hours per day
a	/_/_/ /_/_/ 19/_/_/	/_/_/_/	/_/_/
b	same as above		

2.11 Using the list of the localities, please name main areas where you lived or the closest localities to the place you lived, and also, the following information (*put down all the localities, one per line*)

Area, region	Start date of staying there, duration in 24hr periods and average number of hours per day	Which building did you stay in mostly?
a.	/_/_/ /_/_/ 19/_/_/ /_/_/ /_/_/_/_/ 24hr periods /_/_/ hours per day	1 ☐ in a tent 2 ☐ in a wooden house 3 ☐ brick or concrete house 4 ☐ other, specify 9 ☐ I don't remember
b.	same as above	same as above

2.12 Please, tell me the reasons for your leaving the zone (choose one option).

1 ☐ your radiation dose has exceeded the permissible one
2 ☐ your radiation dose reached the permissible level
3 ☐ your business trip was over
4 ☐ you got sick
5 ☐ other, specify_____
6 ☐ I never left, I am still working there
9 ☐ I don't remember

3. The work conditions in the 30 km zone during the first participation in the activities

The following questions will be related to the methods of dosimetry, means of protection from radiation (if they were at all used) and the type of the work that you were doing when you were in the 30 km zone.

3.1 Was the amount of the radiation dose you received ever estimated (choose one option)?

1 ☐ yes
2 ☐ no
9 ☐ I don't know

If yes, please specify what was the method of estimation of your radiation dose, what was the approximate period of time during which your dose was estimated (*choose "no", "yes" or "I don't know" for each method; if "yes", put down the needed information*). In case your dose was estimated with a personal dosimeter, specify the number of a dosimeter which was used for each period (look at the photo in the booklet).

Method of estimation	Time period	Dosimeter #
With help of personal dosimeter (look at the photo in the booklet)	1 ☐ yes from /_/_/_/_/_/19/_/_/ to /_/_/_/_/_/19/_/_/ from.....to 2 ☐ no 9 ☐ I don't remember	/_/_/ /_/_/
By method of group dosimetry	1 ☐ yes from /_/_/_/_/_/19/_/_/ to /_/_/_/_/_/_/19/_/_/ from.....to 2 ☐ no 9 ☐ I don't remember	
According to the route documents	1 ☐ yes from/_/_/_/_/_/_/19/_/_/ to /_/_/_/_/_/_/_/19/_/_/ 2 ☐ no 9 ☐ I don't remember	

3.2 In case you had a personal dosimeter, how often did you use it (choose one option)?

1 ☐ all the time
2 ☐ only during the time of work
3 ☐ sometimes during work
9 ☐ I don't remember

3.3 Have you been returning the dosimeter to the dosimetry service on a regular basis (choose one option)?

1 ☐ yes
2 ☐ no
9 ☐ I don't remember

If "yes", please tell me how often did you do it (choose one option)?

1 ☐ every day
2 ☐ once a week
3 ☐ once in two weeks
4 ☐ once a month
5 ☐ as often as it was requested by the dosimetry service
9 ☐ I don't remember

3.4 Have you evaluated yourself the radiation dose you got during your work (choose one option)?

1 ☐ yes
2 ☐ no
9 ☐ I don't remember

If "yes", what was the result of your calculations regarding your dose? /_/_/_/_

Put down unit of measurement (choose one option)?

1 ☐ Bar
2 ☐ Rad
3 ☐ Roentgen
4 ☐ other, specify_____
9 ☐ unknown

Your reaction towards the effect of radiation during the time you spent in the 30km zone of Chernobyl power station: did you get more radiation than the others, why do you think so?

_____

_____

_____

3.5 Did you do the following types of work (choose one option in every line)?

Type of work	Yes	No	I don't remember
Participation in building of "Sarcophagus" directly at Chernobyl power station industrial platform	1 ☐	2 ☐	9 ☐
Removing of highly activated fragments and/or graphite pieces from the roofs of the buildings and platforms near ventilation pipes	1 ☐	2 ☐	9 ☐
Deactivation of the premises and equipment at Chernobyl PS	1 ☐	2 ☐	9 ☐

Type of work	Yes	No	I don't remember
Deactivation of industrial platform and the adjacent area, including equipment outside of the Chernobyl power station	1 ☐	2 ☐	9 ☐
Radiation investigation	1 ☐	2 ☐	9 ☐
Deactivation of auto transportation means, etc.	1 ☐	2 ☐	9 ☐
Repairing and servicing Chernobyl PS equipment	1 ☐	2 ☐	9 ☐
Other types of work inside Chernobyl PS area, specify	1 ☐	2 ☐	9 ☐
Deactivation work and burying of radioactive waste outside Chernobyl PS	1 ☐	2 ☐	9 ☐
Building of roads in the 30 km zone	1 ☐	2 ☐	9 ☐
Working as a driver	1 ☐	2 ☐	9 ☐
Being a security guard at Chernobyl PS or in the 30 km zone	1 ☐	2 ☐	9 ☐
Other types of work outside Chernobyl PS area	1 ☐	2 ☐	9 ☐

3.6 Have you ever used the following means of protection during the time of work in the 30 km zone (choose one option in each line)?

Means of protection	Yes	No	I don't remember
Respirator or gas-mask	1 ☐	2 ☐	9 ☐
Gloves	1 ☐	2 ☐	9 ☐
Protective glasses	1 ☐	2 ☐	9 ☐
Protective clothes	1 ☐	2 ☐	9 ☐
Lead apron	1 ☐	2 ☐	9 ☐
Special protective auto transportation means (armored automobiles, lead sheets in helicopters)	1 ☐	2 ☐	9 ☐
Other, specify_____	1 ☐	2 ☐	9 ☐

3.7 Did you work at the Chernobyl power station industrial platform (choose one option)?

1 ☐ yes
2 ☐ no
9 ☐ I don't remember

3.8 Were you given iodine during your working in 30 km zone (choose one option)?

1 ☐ yes
2 ☐ no
9 ☐ I don't remember

If "yes", please put down the time period and the dosage
from /_/_/_/_/_/19/_/_/ to /_/_/_/_/_/19/_/_/
and the quantity of tablets per day /_/_/

3.9 Please, name the people who worked with you.

Last name, first name, patronymic	Position

4. The description of the first episode of work in the 30 km zone of Chernobyl PS during the first time when the liquidator being questioned participated in the activities in the zone

In this part I would like to ask you to remember your everyday work in detail. If you had to work in the 30 km zone during the first days after the incident, in other words, in the end of April or in May, then try to remember the episodes, during which you could have received a substantial dose of radiation.

4.1 Tell me, please, where were you working (use photos and maps/diagrams from the booklet - part B - and also, the decoded marks - pages 16-19-, lists of premises - pages 20-23 - and localities - pages 24-57 - from part A. Choose all the options that apply):

1 ☐ at the Chernobyl PS, inside the premises (fill out section a.)
2 ☐ at the Chernobyl PS, on the rooftops of the buildings (fill out section b.)
3 ☐ outside, at the Chernobyl PS, in the places other than above (fill out section c.)
4 ☐ outside the Chernobyl PS site(fill out section c.)
5 ☐ in means of transportation - work around all the 30 km zone, including the PS site - (fill out section d.)
9 ☐ I don't remember (move to question 4.2)

a. <u>On the Chernobyl PS site inside the premises</u> (if not, move to lines b. and c.):

a.1 Put down the premises where you worked (use schemes and photos from the booklet - part B - and also, decoded marks - pages 16-19 - and lists of premises - pages 20-23- from part A. Choose one number and put it down). /_/_/_/_/_/_/_/_/_/

a.2 How long did it take you to walk to your place of work after you entered the building (put down the time period in minutes)? /_/_/_/_/_/

a.3 Did you walked more than two stair flights?

1 ☐ yes
2 ☐ no

9 ☐ I don't know

a.4 What was the size of the premises you worked in(put down the size in square meters)? /_/_/_/_/_/_/_/_/_/_/

a.5 Were there any windows?

1 ☐ yes
2 ☐ no
9 ☐ I don't remember

a.6 If "yes", were they leaded?

1 ☐ yes
2 ☐ no
9 ☐ I don't know

a.7 What color were the walls (choose one option)?

1 ☐ white
2 ☐ gray
3 ☐ golden
4 ☐ silver
5 ☐ green
6 ☐ brown
7 ☐ other, specify_____
9 ☐ I don't remember

a.8 Were the doors massive (choose one option)?

1 ☐ yes
2 ☐ no
9 ☐ I don't remember

a.9 What was the floor covered with (choose one option)?

1 ☐ plastic
2 ☐ concrete
3 ☐ tiles
4 ☐ tree
5 ☐ other, specify_____
9 ☐ I don't remember

a.10 Was there any cumbersome equipment on the premises (choose one option)?

1 ☐ yes
2 ☐ no
9 ☐ I don't know

a.11 Describe some other details which would characterize your place of work on the premises

_____

_____

_____

b. On the site of the Chernobyl PS on the rooftops of the buildings:

b.1 Which rooftop (of which building) you were working at (use diagrams and photo from the booklet - part B - , choose one number from the map or diagram from pages 2-3 and put it down)? /_/_/_/_/_/_/_/_/

b.2 Were there any other buildings near by (choose one option)?.

1 ☐ yes
2 ☐ no
9 ☐ I don't know

If "yes", put down buildings' numbers from the map/scheme from the booklet: /_/_/_/_/_/_/_/_/_/_/_/_/_/_/_/_/_/_/_/

b.3 Was the rooftop (choose one option)

1 ☐ higher than other buildings?
2 ☐ lower?
9 ☐ I don't remember

b.4 Did it have different levels (choose one option)?

1 ☐ yes
2 ☐ no
9 ☐ I don't remember

b.5 What was the roof size? (put down the size in square meters) /_/_/_/_/_/_/_/

b.6 What was the roof covered with (choose one option)?

1 ☐ concrete
2 ☐ slate
3 ☐ wood
4 ☐ tar
5 ☐ other, specify_____

b.7 Was the roof damaged in any way near the work site (choose one option)?

1 ☐ yes
2 ☐ no
9 ☐ I don't remember

b.8 Were there any wreckage or waste near the work site (choose one option)?

1 ☐ yes
2 ☐ no
9 ☐ I don't remember

b.9 Where was the stairway to the roof (choose one option)?

1 ☐ outside the building
2 ☐ inside the building
9 ☐ I don't remember

b.10 Describe any other details which would characterize the roof work site:_____

_____

_____

c. In open air:

c.1 If you worked on the site of the Chernobyl PS but not on the rooftops of the buildings, put down the number of the closest building to your place of work (use maps and photos from the booklet and put down the number) /_/_/_/_/

c.2 If you worked outside the Chernobyl PS site, then put down the name of the locality (region, district, etc.) that you worked at, or the closest to your place of work (use maps and lists of localities):_____

c.3 Were the following landmarks near your place of work (you may choose a few options)?

1 ☐ buildings
2 ☐ power lines
3 ☐ other landmarks, specify_____
9 ☐ I don't remember

c.4 What kind of equipment was located near your place of work (you may choose a few options)?

1 ☐ bulldozers
2 ☐ dump trucks
3 ☐ excavators
4 ☐ cranes
5 ☐ other equipment, specify_
9 ☐ I don't remember

c.5 What did you have under your feet (choose one option)?

1 ☐ soil
2 ☐ crushed stone
3 ☐ concrete
4 ☐ asphalt
5 ☐ sand
6 ☐ other, specify_____
9 ☐ I don't remember

c.6 Was a "stopping up" of radioactive dust ever conducted at your place of work (choose one option)?

1 ☐ yes
2 ☐ no
9 ☐ I don't remember

c.7 Describe some other details which would characterize your work site:

_____

_____

d. In means of transportation (working around the whole 30 km zone, including the Chernobyl PS site):

d.1 Name the type of mode of transportation that you worked in (choose one option)

1 ☐ bulldozer
2 ☐ bus
3 ☐ dump truck
4 ☐ car
5 ☐ tractor
6 ☐ crane
7 ☐ other, specify____
9 ☐ I don't remember

d.2 Was that mode of transportation equipped with means of protection from radiation (choose one option)?

1 ☐ yes
2 ☐ no
9 ☐ I don't remember

If "yes", describe them:_____

d.3 Describe the routes you were taking: roads, localities, industrial objects (use maps and lists of localities):

_____
_____
_____

4.2 Type of activities in an episode:

a. Tell me, please, in detail about what kind of work did you do and what kind of instruments and devices you used?

_____
_____
_____

b. How did you work (choose one option)?

1 ☐ in group
2 ☐ alone
9 ☐ I don't remember

c. Did you work at the "burial sites" (choose one option)?

1 ☐ yes
2 ☐ no
9 ☐ I don't remember

4.3 How did you get to work in an episode:

a. What type of transportation did you usually use to get to your place of work and back (choose one option)?

1 ☐ armoured troop carrier
2 ☐ bus
3 ☐ tractor
4 ☐ helicopter
5 ☐ car
6 ☐ truck
7 ☐ other, specify____
9 ☐ I don't remember

b. Describe the route you took to your place of work and back (choose one option)":

where were you coming from_____

where were you heading_____

landmarks along your route_____

c. Did you transfer from one transportation to another (choose one option)?

1 ☐ yes
2 ☐ no
9 ☐ I don't know

If "yes", put down the points at which you transferred_____

d. How much time did it take you to get from the place you lived at to work and back (put down the time period in minutes)? /_/_/_/_/_/_/_/

e. Additionally, did you have to walk to work after you got off the transportation (choose one option)?

1 ☐ yes
2 ☐ no
9 ☐ I don't remember

If "yes", put down the time period in minutes /_/_/_/_/_/_/

f. Describe the route you took on the way back from work:

where were you coming from _____

where were you heading_____

landmarks along your route_____

4.4 Food and rest during the time of work in the episode

a. Where did you eat during the time of work (use maps and photos from the booklet - part B)?

1 ☐ outside of the premises (put down buildings' numbers from the maps or diagrams, or the name of the locality):_____

2 ☐ on the premises (put down the building numbers from the map or diagrams, or the name of the locality):_____

3 ☐ inside the transportation (specify the type):_____

9 ☐ I don't remember

b. How did you get to the place where you ate (choose one option)?

1 ☐ on foot
2 ☐ by transportation
9 ☐ I don't remember

If by transportation, put down how much time it took to get to the destination (put down the time period in minutes) /_/_/_/

and the route you took_____

c. How much time did you have for lunch (put down the time period in minutes)? /_/_/_/_/

d. Where did you rest during your breaks (use maps and photos from the booklet and choose one option)?
   1 ☐ outside the premises (put down building numbers from the map and diagram 2-3):_____
   2 ☐ inside the premises (put down building numbers from the map and diagram 2-3, or the name of the locality):_____
   3 ☐ inside the transportation (specify the type):_____
   9 ☐ I don't remember

e. How did you get to the place of rest (choose one option)?
   1 ☐ on foot
   2 ☐ by transportation
   9 ☐ I don't remember

If by transportation, specify how much time it took you to get to your destination (put down the time period in minutes)? /_/_/_/_/
and the route you took_____

f. How much time during the working day did you spent resting (put time amount in minutes)? /_/_/_/

4.5 Time spent working in the episode:
from/_/_/ /_/_/19/_/_/ to /_/_/ /_/_/19/_/_/

Working days in the episode: (*mark by pen only those dates in the calendar which correspond to the working days of the liquidator in April-June of 1986 and the months starting from July of 1986 to the end of 1987*)
(NB! Please note that, according to the Slavic calendar, the week starts with Monday, not Sunday)

April/May of 1986						
Monday	Tuesday	Wed.	Thurs.	Friday	Sat.	Sunday
21	22	23	24	25	26	27
28	29	30	1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30	31	

June of 1986						
Monday	Tuesday	Wed.	Thursday	Friday	Saturday	Sunday
						1
2	3	4	5	6	7	8
9	10	11	12	13	14	15
16	17	18	19	20	21	22
23	24	25	26	27	28	29
30						

1986	1987	
July	January	July
August	February	August
September	March	September
October	April	October
November	May	November
December	June	December
December	July	December

4.6 Number of the hours you worked per day (average) /_/_/_/_/

4.7 Dosimetry control in the episode:

a. Did you change before work (choose one option)?
   - 1 ☐ yes
   - 2 ☐ no
   - 9 ☐ I don't remember

b. Did you start working as soon as you would arrive (choose one option)?
   - 1 ☐ yes
   - 2 ☐ no
   - 9 ☐ I don't remember

If "no", put down the time period in minutes you would spend before work /_/_/_/_/

c. Did you have to pass a point of control ("KPP") to estimate the level of radioactive contamination (choose one option)?
   - 1 ☐ yes
   - 2 ☐ no
   - 9 ☐ I don't remember

d. Did you put your feet in containers with manganese solution (choose one option)?
   - 1 ☐ yes
   - 2 ☐ no
   - 9 ☐ I don't remember

e. Did the dosimetry specialist control the work process or was he around during your work (choose one option)?
   - 1 ☐ yes
   - 2 ☐ no
   - 9 ☐ I don't remember

f. Was the supervisor of the work process in contact with the dosimetry specialist (choose one option)?
   - 1 ☐ yes
   - 2 ☐ no
   - 9 ☐ I don't remember

g. Was the dosimetry specialist a military officer (choose one option)?

1 ☐ yes
2 ☐ no
9 ☐ I don't remember

4.8 Your comments regarding the episode;

a. Do you think that the work process you've described was well organized and "tightly" controlled by your supervisor, the dosimetry specialist, etc. (choose one option)?
   1 ☐ yes
   2 ☐ no
   9 ☐ I don't remember

b. What was the most memorable moment during the time of work?

_____

_____

_____

c. Please, comment on anything else connected with the work you did in the episode.

_____

_____

5. General information regarding professional activities

Now I am going to ask you a few questions regarding your profession and possible unhealthy work conditions which you experienced, if applicable.

5.1 In the present, what professional group do you belong to (choose one option)?

1 ☐ student
2 ☐ farmer
3 ☐ industrial worker
4 ☐ administrative worker
5 ☐ freelance work
6 ☐ unemployed
7 ☐ not-working invalid or retired
8 ☐ other, specify_____

5.2 What professional group did you belong to before participating in the "clean-up" activities at the Chernobyl PS (choose one option)?

1 ☐ student
2 ☐ farmer
3 ☐ industrial worker
4 ☐ administrative worker
5 ☐ freelance work
6 ☐ unemployed
7 ☐ not-working invalid or retired
8 ☐ other, specify_____

5.3 Have you ever performed any work connected with radiation except for the one you performed during the "clean-up" work at the Chernobyl PS (choose one option)?

1 ☐ yes
2 ☐ no
9 ☐ I don't remember

If "yes", please specify the district of your professional activities, dates of work, name and location of the organization which you worked at (choose "yes" or "no" for every sphere of professional activities, if "yes", specify the necessary information).

Sphere of professional activities	Work period, month/year	Organization (name, location)
Medicine	1 ☐ yes from....to from....to from....to 2 ☐ no	....
Nuclear industry (including PS)	1 ☐ yes from....to from....to from....to 2 ☐ no	....
Industrial radiography	1 ☐ yes from....to from.....to from....to 2 ☐ no	....
Army service as opposed to the above-mentioned occupations	1 ☐ yes from....to from....to from....to 2 ☐ no	....
Other, specify	1 ☐ yes from....to from...to from....to 2 ☐ no	....

5.4 Have you ever worked at any of these "unhealthy" industrial productions (*show the list of these productions to the liquidator you are interviewing*), including the time you served in the Army (choose one option)?

1 yes
2 no
9 I don't remember

If "yes", please specify the production, dates of work, name and location of the organization which you worked at.

Production	Work period, month/year and work title	Organization (name, location)
....	from .....to	....
....	from.....to	....

5.5 Have you ever worked with any of these "unhealthy" chemical substances (*show the list of these substances to the liquidator whom are interviewing; choose one option*)?

1 yes
2 no
9 I don't remember

If "yes", please specify the chemical substance, dates of work, name and location of the organization which you worked at.

Chemical substance	Work period, month/year	Organization (name, location)
_____	from.....to	_____
_____	from.....to	_____
_____	from.....to	_____

6. Medical history

Now, try to remember whether you have ever been diagnosed with illnesses which I am going to ask you about.

6.1 Have you ever had problems with your thyroid (choose one option)?

1 yes
2 no
9 I don't remember

If "yes", please, specify the following information:

Name of the disease	Year it was diagnosed	Hospital, its address (district, region)
Goitre	19/ / /	
Changes in (lymphatic)knots	19/ / /	
Hypoterios	19/ / /	
Hyperterios	19/ / /	
Thyroidit	19/ / /	
Other, specify	19/ / /	

6.2 Has a doctor ever told you that you have a tumor (benign or malignant) or leucos (choose one option)?

1 ☐ yes
2 ☐ no
9 ☐ I don't remember

If "yes", please specify (put down for every tumor separately: first localization, hospital, where you were diagnosed, year of the first diagnosis and choose answers corresponding to the treatments you received).

a. First tumor

Localization_____

Hospital_____

Year of the diagnosis 19/_/_/

Treatment:	Yes ☐	No ☐	I don't remember ☐
Radiation therapy	1 ☐	2 ☐	9 ☐
Chemotherapy	1 ☐	2 ☐	9 ☐
Surgical operation	1 ☐	2 ☐	9 ☐
Other, specify____	1 ☐	2 ☐	9 ☐

b. Second tumor

Localization_____

Hospital_____

Year of the diagnosis 19/_/_/

Treatment:	Yes ☐	No ☐	I don't remember ☐
Radiation therapy	1 ☐	2 ☐	9 ☐
Chemotherapy	1 ☐	2 ☐	9 ☐
Surgical therapy	1 ☐	2 ☐	9 ☐
Other, specify____	1 ☐	2 ☐	9 ☐

6.3 Have you ever been treated with radiation therapy for other illnesses, which were not listed in question 6.1 (choose one option)?

1 ☐ yes
2 ☐ no
9 ☐ I don't remember

If "yes", please specify:

illness_____

hospital where you were treated with radiation therapy_____

year of treatment with radiation therapy 19/_/_/

6.4 Have you ever gone through the following x-ray tests (choose "no", "yes" or "I don't remember" for every x-ray test; if "yes", specify the number of the tests you took)?

X-ray tests		**Number of tests**
X-ray of teeth	1 ☐ yes, specify how many times	/_/_/_/
	2 ☐ no	
	9 ☐ I don't know	

9. Alcohol consumption

9.1 Presently, how often do you drink alcohol (choose one option)?

1 ☐ never
2 ☐ once a month or less
3 ☐ 2-3 times a week
4 ☐ once a week
5 ☐ a few times a week
6 ☐ every day

If you drink alcoholic beverages, then please tell me whether you usually drink the following drinks and how much do you drink per day (average)?

Alcoholic beverage		**Quantity (in milliliters)**
Beer	1 ☐ yes, specify 2 ☐ no	/_/_/_/_/
Vodka, including home-distilled vodka	1 ☐ yes, specify 2 ☐ no	/_/_/_/_/
Wine	1 ☐ yes, specify 2 ☐ no	/_/_/_/_/
Other, specify_____	1 ☐ yes, specify 2 ☐ no	/_/_/_/_/

9.2 Did you change your habits regarding alcohol consumption after your work at the Chernobyl PS zone (choose one option)?

1 ☐ nothing changed
2 ☐ now I drink more
3 ☐ now I drink less
4 ☐ I started to drink more after Chernobyl
5 ☐ now I don't drink at all

10. Conclusion

10.1 Thank you for answering my questions. If you'd like to add anything, please put down anything you find necessary.

_____

_____

_____

_____

Time when the interview was finished:

_____ **hours/_/_/ minutes/_/_/**

11. Questions to the interviewer

11.1 The place of conducting of the interview (choose one option)

1 ☐ clinic
2 ☐ other, specify_____

11.2 Did the respondent answer your questions eagerly (choose one option)?

1 ☐ no (was uninterested, secretive)
2 ☐ was somewhat interested and communicative
3 ☐ was very interested and was trying to help as much as he could

11.3 How well, do you think, the liquidator remembers the details of his work in the 30 km zone (choose one option)?

1 ☐ very well
2 ☐ well
3 ☐ well enough
4 ☐ poorly
5 ☐ doesn't remember at all

11.4 If the liquidator answered that he worked in the area of the Chernobyl PS, how sure are you that his answer is correct (*one needs to take into account the descriptions provided by the liquidator: of his work in the area, of the maps, diagrams and photos which you provided him with*)?

1 ☐ absolutely sure
2 ☐ not sure
3 ☐ I think that the liquidator didn't work in the area of the Chernobyl PS
8 ☐ the liquidator told me that he didn't work in the area of the Chernobyl PS
9 ☐ I don't know

explain why do you think so

_____

_____

_____

11.5 How well does the liquidator remember the details of how he was irradiated as a medical treatment or at the industrial production (choose one option)?

1 ☐ very well
2 ☐ well
3 ☐ well enough
4 ☐ poorly
5 ☐ doesn't remember at all

11.6 How well does the liquidator remember the details of the way the chemical substances affected him when he was treated in the hospital or at the industrial production (choose one option)?

1 ☐ very well
2 ☐ well
3 ☐ well enough
4 ☐ poorly
5 ☐ doesn't remember at all

11.7 Please, add your comments regarding the answers of the liquidator to the questionnaire and, also, on the interview in general. In particular, specify details and facts which didn't find any reflection in the questionnaire, but which were told to you by the liquidator and which you find important to mention; specify any details regarding the liquidator's state of mind, which could affect his answers (for example, was he/she sick, maybe, he/she was having some problems at the time, or he/she was in a hurry during the interview).
